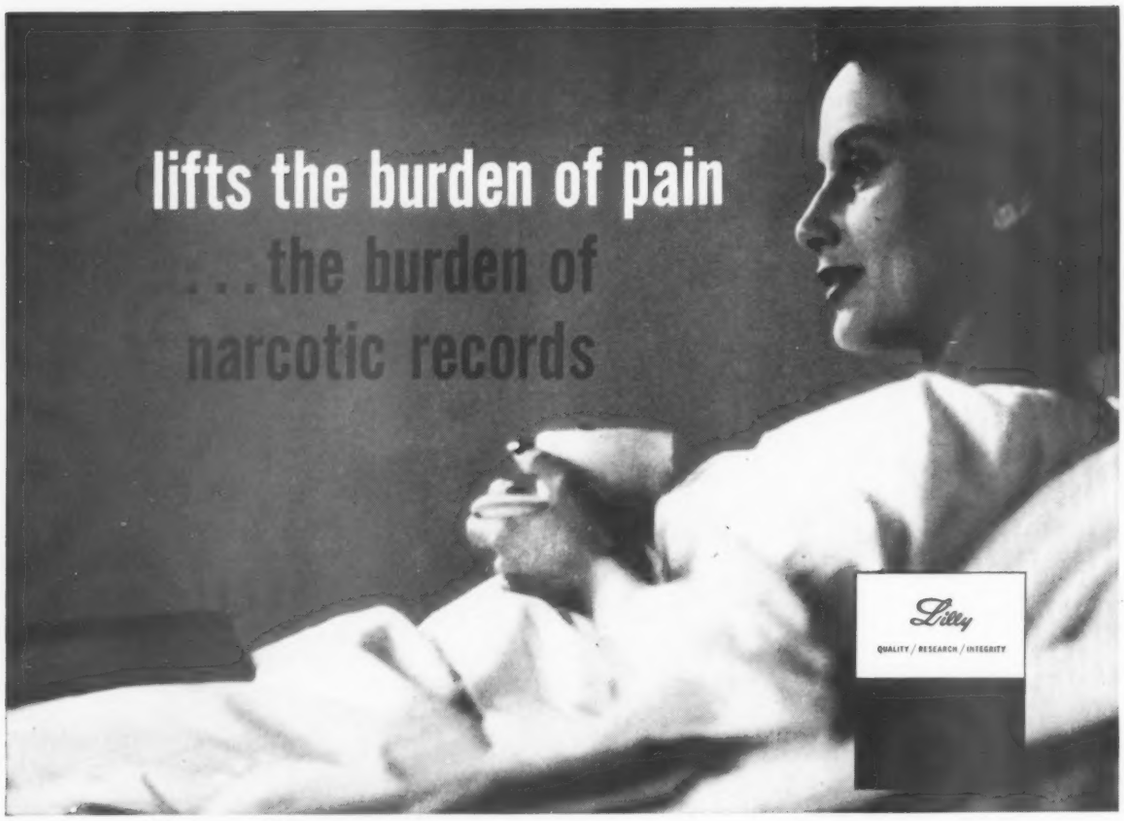
vol 16 no 3 MARCH 59

American Journal of Hospital Pharmacy

Official publication of the American Society of Hospital Pharmacists

FORMERLY The BULLETIN

the LEGAL RESPONSIBILITY OF THE HOSPITAL PHARMACIST in the United States



DARVON® COMPOUND

The clinical usefulness of Darvon® (dextro propoxyphene hydrochloride, Lilly), alone and in combination, has been confirmed by more than a hundred investigators in the treatment of over 6,300 patients. Under study were patients from every branch of medicine, including obstetrics, gynecology, surgery, orthopedics, and oncology.

Consolidation of these reports shows that 5,663 patients (89.9 percent) obtained effective analgesia. The remaining 637 patients (10.1 percent) were not benefited.

In the hospital, the use of Darvon and Darvon Compound provides the additional advantage of convenience for the hospital staff. A narcotic prescription is not required; physicians may prescribe them without the need for special records or time-consuming bookkeeping.

Each Pulvule® Darvon Compound provides:

Darvon	32	mg. (approx. 1/2 gr.)
Acetophenetidin	162	mg. (2 1/2 grs.)
A.S.A.® (acetylsalicylic acid, Lilly)	227	mg. (3 1/2 grs.)
Caffeine	32.4	mg. (1/2 gr.)

Usual dosage: 1 or 2 Pulvules three or four times daily.

Also available: Darvon, in 32 and 65-mg. Pulvules.

Usual dosage: 32 mg. every four hours or 65 mg. every six hours.

Darvon® Compound (dextro propoxyphene and acetylsalicylic acid compound, Lilly)

ELI LILLY AND COMPANY • INDIANAPOLIS 6, INDIANA, U.S.A.

920209

Dear Sirs:

Of Historical Interest

DEAR SIRS: Congratulations on the November issue of the AMERICAN JOURNAL OF HOSPITAL PHARMACY which seemed even better than usual. I think your editorial and article on the need for a pharmaceutical abstract service were good, constructive and influential.

In connection with the JOURNAL, I am wondering what you do with glossy photographs of probable historical interest after engravings have been made? I am constantly surprised how difficult it is to obtain glossy photographs of important events and people in action some years later. And it is not nearly so satisfactory to copy pictures from the printed page of old journals.

If you do not maintain a classified "morgue" of photographs, I hope you will remember on occasion to send us pictures that seem to depict events and people of lasting interest. . .

GLENN SONNEDECKER, *Director*

American Institute of the History of Pharmacy
University of Wisconsin
School of Pharmacy
Madison 6, Wisconsin

EDITOR'S NOTE: Photographs of significant events and important men in action in American pharmacy, may be sent for deposit to the American Institute of the History of Pharmacy. Please date and identify each photograph as accurately as possible (by a label pasted on the back), marking uncertain information with a question mark.

Journal Articles Requested

DEAR SIRS: In an abstract appearing in the October, 1958 issue of the AMERICAN JOURNAL OF HOSPITAL PHARMACY, reference is made to an article entitled "Improving the Method of Preparation of Sterile Blood Serum for Medicinal Preparations." . . . the subject interests me and I wonder if a translation of the article is available?

Might I add that we value highly your JOURNAL and consider it one of the most helpful publications in the field . . .

A. E. ALDRIDGE, *Manager*

I.V.S. Unit
Auckland Public Hospital
Auckland, New Zealand

DEAR SIRS: We would like to receive a copy of the article on iodophors as sanitizers which appeared in THE BULLETIN OF THE AMERICAN SOCIETY OF HOSPITAL PHARMACISTS (March-April, 1955) issue . . .

G. VOURLACOS AND COMPANY

Athens, Greece

Appreciation

DEAR SIRS: Once again, I want to express my appreciation to you for the fine layout of the recent article entitled "Around-the-Clock Pharmacy Service." Perhaps one of the reasons the JOURNAL is so outstanding is because of the layout and plan of each article.

LOUIS P. JEFFREY, *Pharmacist-in-Chief*

Albany Hospital
Albany, New York

Compliment

DEAR SIRS: . . . I would like to add that the new format of the AMERICAN JOURNAL OF HOSPITAL PHARMACY is quite an asset. You and your co-workers deserve a lot of credit. Keep up the good work. Thank you again.

SISTER ANNE GALLAGHER, *Pharmacist*

St. Bernard's Hospital
Chicago 21, Illinois

Interest in Antibiotic Symposium

DEAR SIRS: I have read with interest the summary of the Sixth Annual Symposium on Antibiotics which appeared in the December (1958) issue of your JOURNAL. I would be grateful if you could advise me if a reprint is available . . .

J. E. MATTHEWS, *Health Supplies Officer*

Civil Defense Health Services
Department of National Health and Welfare
Ottawa, Canada

when you prescribe CARBRITAL®

pentobarbital sodium and carbromal •
in Kapseals® and Elixir form

you prescribe sleep

PARKE, DAVIS & COMPANY • DETROIT 32, MICHIGAN

70459

editorial

by DON E. FRANCKE

AHA-ASHP Statement on Pharmacy and Therapeutics Committee

► HOSPITAL PHARMACISTS WILL READ WITH MORE than passing interest the "Statement on the Pharmacy and Therapeutics Committee" and the statement on "Suggested Principles of Relationship Between Smaller Hospitals and Part-Time Pharmacists Who Provide Pharmaceutical Service" which are contained in this issue of the JOURNAL beginning on pages 122 and 124. These statements assume great significance since they have been approved by and represent the official positions of the Board of Trustees of the American Hospital Association and the Executive Committee of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS.

The statement on the Pharmacy and Therapeutics Committee is the first of a series of two or more statements related to the Formulary System in hospitals which is being drafted by the members of the Joint Committee of the American Hospital Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. The objective of these statements is to provide hospital administrators, physicians, and pharmacists with a clearly prepared set of principles related to the Formulary System and its operation. As will be noted, the Statement on the Pharmacy and Therapeutics Committee is an expansion and elucidation of one of the main points contained in the Minimum Standard for Pharmacies in Hospitals. It is hoped that these new statements will enable all concerned to approach the operation of the Formulary System in a sound, objective manner.

Need for these statements has been stimulated by the appearance of the American Hospital Formulary Service. The enthusiastic response shown by hospitals and their staffs to this Service is indicative of the need for, an interest in, such a compilation of drug monographs as is now being furnished by the SOCIETY. Appearance of the ASHP Formulary Service plus a series of statements relative to the operation of the Formulary System should stimulate hospitals to review their entire body of policies and procedures relative to the handling and use of drugs. The advisory and educational functions of the Pharmacy and Therapeutics Committee should be especially noted. The points noted under "Organization" should be given careful consideration so that a reasonable method of procedure may be evolved for handling all questions related to drugs. The section devoted to "Functions and Scope" merits careful study for it is in this area that many Pharmacy and Therapeutics Committees falter. Too often, the functions and scope of the Pharmacy and Therapeutics Committee are viewed only in terms of the preparation of a formulary. It is very important that this concept be broadened to include recommendations of broad professional policies regarding the evaluation, selection, procurement, distribution, use, safety practices and other matters pertinent to drugs in hospitals.

It is not intended that all hospitals will adopt identical procedures for the operation of the Formulary System. This is neither necessary nor desirable. However, the principles of operation should be essentially the same in all hospitals. A well-operated formulary system must be guided by principles which are just and fair to the patient, the medical staff, the pharmacy staff, and the hospital. Especially important is the spirit with which the system is operated. If the pharmacist, on whom falls the responsibility of implementing the formulary system, maintains an attitude of helpful cooperation with the medical staff, if he fosters the formulary system as an educational tool for practitioners and students of medicine, nursing and pharmacy, if he encourages the acceptance and use of really new and better drugs as they are developed and evaluated, and if he employs the formulary system to actively promote better patient care—if he does these things and is guided by sound professional principles, the formulary system in his hospital will be well accepted by all.

THE LEGAL RESPONSIBILITY of the hospital pharmacist in the United States

by GEORGE F. ARCHAMBAULT

► IT IS NOT ONLY A PRIVILEGE BUT A DISTINCT HONOR for me to have been invited to address this international federation of pharmacy on the subject "The Legal Responsibility of the Hospital Pharmacist." I thank you sincerely for inviting me to participate with such a distinguished panel of associates.

Obviously, one cannot in the time allotted hope to cover the major principles of law and the Statutes and Codes that have an impact upon pharmaceutical services in hospitals of any land.

Background to Hospital Pharmacy Law

In 1954 in Chicago, it was my pleasure to bring together for an Institute on Hospital Law of the American Hospital Association, many of the major elements of Federal and state laws, statutes, and codes applicable to hospital pharmacy practice in the United States. This compilation was eventually published in *The Bulletin of the American Society of Hospital Pharmacists,* Vol. 14, May-June, 1957, an issue now referred to as "The Law Number." That presentation covered, among other things, the subjects of charitable trust doctrines, police laws in relationship to registration and licensing of health professionals, the hiring of hospital pharmacists, the hiring and utilization of nonprofessionals, the degree of skill and care required of a hospital pharmacist, the legal impact of minimum standards and procedure manuals upon a specific code of conduct, legal liabilities in connection with P.R.N. and standing orders, signas and age of patient on the written prescription of the physician.

The discussion also included the fundamental elements required to establish negligence in tort cases and the elements necessary to prove breach of contract, inasmuch as the paper was also aimed at nonlawyers, more specifically hospital administrators, trustees and pharmacists, as well as attorneys interested in the law of hospitals.

Malpractice and product liability insurance, pharmaceutical patents, prescriptions as privileged communications, ownership of the prescription, the substitution and duplication problem in the United States, Fair Trade Laws, the Federal Food and Drug Laws, legal principles concerning the use of investigational drugs in hospitals, and the U. S. Alcohol, Narcotic and similar Codes concluded the discussion. This material has been further developed over the past five years so that at present this "high-lighting" of legal material of interest to hospital pharmacists is now presented in graduate schools of pharmacy in the United States in four one-hour lecture periods. I have with me reprints of the original paper for those

GEORGE F. ARCHAMBAULT, Ph.C., D.Sc., LL.B., is a Member of the Massachusetts Bar, Pharmacist Director, Chief, Pharmacy Branch, Division of Hospitals, Department of Health, Education, and Welfare, U. S. Public Health Service, Washington, D. C.

Presented at the meeting of FEDERATION INTERNATIONALE PHARMACEUTIQUE, Brussels, Belgium, September, 1958.

of you who are interested in having a copy for your files. This presentation today covers the common law points (case law) of that paper but none of the United States or State Statutes or Codes. Today's presentation brings up to date, as best I can, the common law in the 1954 paper to current United States law, as it pertains to the legal responsibility of the hospital pharmacist in the United States.

Six Main Points

Today, I propose to speak to some 6 main issues: (1) the charitable trust immunity doctrine in the United States; (2) the law of negligence in tort and criminal cases, especially as negligence principles are applied to the handling of items that are inherently dangerous such as medications, (3) the much talked about "new" application of the doctrine of implied warranty for fitness for use or merchantability in sales, resulting from the recent Cutter polio suits in California, (4) malpractice insurance, (5) investigational drugs in hospitals, and (6) the legal effect of patents upon the pharmacist practitioner who compounds preparations official in the *United States Pharmacopeia* and *National Formulary*. All of these, of course, in their application to hospital pharmacy practice in the United States and the pharmacist's legal responsibility to his hospital and to himself.

Charitable Trust Immunity Doctrine

The doctrine declaring charitable institutions immune from liability was first declared in the United States in 1876. A recent New York case, Bing *vs.* St. John's Episcopal Hospital (1957) summarizes the 1876 Massachusetts case as follows: (McDonald *vs.* Massachusetts General Hospital 120 Mass. 432) "deciding that a charity patient, negligently operated upon by a student doctor, could not hold the hospital responsible, the court reasoned that the public and private donations that supported the charitable hospital constituted a trust fund which could not be diverted." As sole authority for its conclusion, the Massachusetts Court relied on an English case (Holliday *vs.* St. Leonard's 11 C.B. (N.S.) 192, 142 Eng.-Rep. 769), which was based on a *dictum* in a case decided in 1839 (Duncan *vs.* Findlater, 6 Cl. & Fin. 894 - 7 Eng-Rep. 934), *without apparently observing that the dictum had been overruled* (Mersey Docks *vs.* Gibbs, L.R. 11 H.L. Cas. 686) *and that the decision in the other had been reversed* (Foreman *vs.* Mayor of Canterbury, L.R. 6 Q.B. 214). At any rate, after the McDonald case was decided (Supra, 120 Mass. 432), other courts in the United States though not all on the same theory or for the same reason, followed the lead of Massachusetts in exempting the charitable hospital from liability.

This historical legal gem prompted one court in the United States which recently abandoned the immunity doctrine to say "ordinarily, when a court decides to modify or abandon a court made rule of long standing, it starts out by saying that the reason for the rule no longer exists." In this case, it is correct to say that the "reason" originally given for the rule of immunity never did exist (Pierce *vs.* Yakima Valley Memorial Hospital Association, 43 Wash. 2d 162, 167).

To grasp the full significance of this doctrine and its application in the several states of the United States, one must recall that, as previously pointed out, it has been traditional in the United States for the courts to protect charitable trusts in order to safeguard the funds for their original purposes. Later, as the trustees of the hospitals sought protection for trust funds from the ravages of law suits, by insurance and otherwise, some state courts relinquished responsibility for protecting the assets of eleemosynary corporations. Whether the use of insurance protection came first or the relaxation of the doctrine of charitable immunity is immaterial. Today, but a minority of the states in the United States still holds strictly to the old charitable trust doctrine. There appears to be a definite trend away from the old theory that a charitable hospital cannot be held liable for injuries to its patients caused by the negligence of its employees.

To illustrate how the doctrine applies in states with non-relaxed doctrine, I present here a Massachusetts Pharmacy Practice Case.

"Roosen *vs.* Peter Bent Brigham Hospital, 235 Mass. 66, a case where corrosive sublimate was substituted for epsom salts. On an action to hold the hospital for corporate negligence in the selection of servants, the court stated, "if a hospital is to be held responsible for negligent treatment of patients, there seems to us to be no sound ground for distinction between the negligence of the managers of the hospital and the negligence of subordinate servants as a basis of liability. A sound ground for distinction between exoneration from liability for the negligence of managers and that of subordinate servants seems equally wanting. Since it is settled that there is no liability for negligence of the latter, it must follow that there is none for that of the former . . . The inevitable result of our own decisions is to relieve a hospital from liability for negligence of the managers in selecting incompetent subordinate agents, as well as for the negligence of such subordinate agents selected with care."

Bing Case Overrules Previous Law in N. Y. State

To illustrate how the states of the United States are moving away from this doctrine, I refer again to the recent State of New York Court of Appeals case —Bing *vs.* St. John's Episcopal Hospital (Bing *vs.* St. John's Episcopal Hospital, 2 N.Y. 2d 656, 163 N.Y. S 2d 11). This case, decided only last year (1957), overruled previous law in New York State on its charitable trust immunity doctrine. Prior to the Bing

case, Schloendorff *vs.* New York Hospital, 211 N. Y. 125 was considered the ruling law. The Schloendorff case developed in New York State the principle of law making the liability of a hospital for injuries suffered by a patient, through the negligence of its employees, depend on whether the injury producing act was "administrative" or "medical."

In the Bing case, the plaintiff was severely burned during the course of an operation, performed at St. John's Episcopal Hospital by her physician, for correction of a fissure. The patient had been made ready for the operation, before the surgeon's appearance, by the hospital anesthetist and by two nurses also in the employ of the hospital. Preparatory to administering spinal anesthesia, the anesthetist painted the lumbar region of the patient's back with an alcoholic antiseptic, Tincture of Zephiran (Benzalkonium Chloride), a flammable liquid, reddish in color. Again, after induction of the spinal anesthesia, one of the nurses applied the Zephiran solution to the operative area. Three layers of sheeting were under the patient.

The nurses were fully aware that the flammable antiseptic employed was potentially dangerous. They acknowledged that they had been instructed, not only to exercise care to see that none of the fluid dropped on the linens, but to inspect them and remove any that had become stained or contaminated. However, they made no inspection, and the sheets originally placed under the patient remained on the table throughout the operation.

The surgeon was not in the operating area when the antiseptic was applied and at least 15 minutes elapsed before he initiated the pre-operative draping process. The draping completed, the doctor took a heated electric cautery and touched it to the fissure to mark it before beginning the actual searing of the tissue. As he was about to start the operation itself, there was a smell of very hot singed linen and, without waiting to see a flame or smoke, he doused the area with water. Assured that the fire was out, he proceeded with the operation. Subsequent examination of the patient revealed severe burns on her body. Later inspection of the linen revealed several holes burned through the sheet under her.

In an action against the hospital and the surgeon to recover for the damages suffered, there was a verdict against both. As to the hospital, the lower court charged that the defendant could be held liable *only* if plaintiff's injuries occurred through the negligence of one of its employees while performing an "administrative" as contrasted with a "medical" act. Upon appeal to the Appellate Division, the Court ruled that the application of the antiseptic was in preparation for the operation and therefore part of the operation itself, and therefore a "medical" act making the hospital non-liable. The plaintiff appealed the case to the Court of Appeals in New York. The hospital based its defense on the grounds that the act was a "medical" act and according to the rule in the Schloendorff case, the doctrine of *respondent* superior (let the master respond or be liable) did not apply.

The Court in working around to its decision pointed out that the distinction of medical and administrative acts had *"long plagued the courts."* For example, it was pointed out that the placing of an improperly capped hot water bottle on a patient's body was an administrative act for which the hospital was liable (Iacono *vs.* New York Polyclinic Medical School and Hospital, 296 New York 502), while keeping a hot water bottle too long on a patient's body was a "medical" act for which the hospital was not liable (Sutherland *vs.* New York Polyclinic Medical School and Hospital 298 N.Y. 682). And again, employing an improperly sterilized needle for a hypodermic injection was an administrative act for which the hospital was liable (Peck *vs.* Towns Hospital, 275 App. Div. 302), while improperly administering a hypodermic injection was a medical act for which the hospital was not liable (Bryant *vs.* Presbyterian Hospital in City of New York, 304 N.Y. 538).

The high court in finding for the plaintiff Bing, did away with distinguishing between "medical" and "administrative" acts and stated that "hospitals should in short, shoulder the responsibilities borne by everyone else. There is no reason to continue their exemption from the universal rule of *respondent superior*. The test should be, for these institutions, whether charitable or profit making, as it is for every other employer, was the person who committed the negligent injury-producing act one of its employees and, if he was, was he acting within the scope of his employment?"

Police Laws

We all know that governments have the right to enact laws to protect the life, health, and welfare of their people. These laws are commonly referred to as the laws under the police power of a state and include among others, the statutes covering licensing of physicians, dentists, nurses, pharmacists, and others, as well as the licensing of hospitals, community pharmacies, and laws controlling traffic in narcotics, hypnotics, other drugs and foods.

With these two points—charitable trust doctrine trends in the United States and the need for police laws for the life and health of the citizentry in the licensing of pharmacists and pharmacies—as background material, let us first consider several additional points.

The Hiring of Hospital Pharmacists

In practice, the hospital administrator and chief pharmacist should insist that applicants for pharmacist positions show (a) proof of licensure in the state, and (b) proof of professional competency and good moral

character as indicated by communications with previous employers and medical, dental, nurse, and pharmacist associates who have *recent personal knowledge* of the professional capabilities of the applicant. Also, previous hospital pharmacy experience of good quality is highly desirable.

A three to six month probation period satisfactorily completed, would be further evidence of lack of negligence by the hospital or chief pharmacist in the selection of the bench or staff pharmacist. Should an accident then occur, a charge of negligence might successfully be defended in some states in the United States, depending upon the "tightness" of the state's charitable trust immunity doctrine. In Connecticut, for example, when it is proven that due diligence and care attend the selection of the employee, *no* liability attaches to the hospital for negligence of its employees under the charitable immunity rule of that state. In a Connecticut case, several years ago, a pharmacist permitted a helper to fill nursing station medication containers. Boric Acid was substituted for dextrose. Five infants died as a result. The pharmacist's qualifications had been thoroughly scrutinized before he was employed. The Connecticut Court held the hospital *not liable* for the negligence of *carefully selected employees*. Failure to provide proper facilities, space, and safeguards in the pharmacy was immaterial in this instance. However, some states in the United States require proper labeling of drugs and poisons, and failure to comply or to furnish reasonable safeguards and precautionary measures may well constitute legal negligence. In effect then, a beneficiary patient of a charitable hospital injured in an accident resulting from negligence, may recover if the state *does not have a strict* charitable immunity rule on the books such as in Massachusetts and several other States.

Utilization of Nonprofessional Personnel, Pharmacy Helpers and Others

The use as pharmacists of pharmacy helpers and others such as nurses, not skilled and experienced in the practice of pharmacy as certified by state registration is a criminal offense. In this connection, it is pointed out that an administrator and hospital are not relieved by law of their responsibilities where one pharmacist is employed and the workload is so great that helpers must perform duties which state laws restrict to registered practitioners of pharmacy. As reasonable men, the administrators and trustees of the hospital know or should know the workload could not be handled by the number of pharmacists employed. The same principle of law applies also to the chief pharmacist who utilizes lay personnel improperly.

Criminal Negligence

Excerpts from the inquest report of Judge Donald B. Mayberry of the District Court of the City of Newton, Massachusetts speaks precisely to this issue.

"At an inquest duly holden before the District Court on the 10th day of July, in the year of our Lord one thousand nine hundred and fifty six, in accordance with the provision of Chapter thirty-eight of the General Laws of said Commonwealth, to inquire into the cause and manner of the deaths of _____ and _____ and whose dead bodies have been found lying in the City of _____ and within the jurisdiction of said Court; and whose deaths are supposed to have been caused by acts of violence committed within the County.

"The Presiding Justice of said Court, having been duly notified of the deaths and of the circumstances attending the same by _____, the Acting Medical Examiner of the County of _____, after hearing the testimony relating to the cause and manner of said deaths, finds that they came to their deaths at said City of _____ on the 10th day of June, in the year of our Lord one thousand nine hundred and fifty six, *in consequence of Sodium Nitrite poisoning due to ingestion of a solution of Sodium Nitrite removed from a container labeled 'Phospho Soda'*, and that the criminal negligence set forth hereinafter, contributed thereto.

"It is not the intention of the Court to go into detail concerning how these tragedies occurred, by reason of the fact that the record itself, a copy of which is filed herewith, speaks far more eloquently concerning that matter, than any words of mine could hope to explain.

"Suffice to say, however, a study of the evidence reveals acts of carelessness, carefree abandonment of responsibilities, the delegation of responsibilities to others, certain omissions to act, and wanton and reckless acts, as well as incompetence and the failure to qualify for the jobs they were intended to do on the part of the Director of the _____ Hospital; the Chief Pharmacist of the _____ Hospital; and the pharmacist's helper so as to warrant and justify a *finding of criminal negligence* on the part of the above named and described individuals, and by reason thereof, *that is the finding of the Court.*

"The _____ Hospital has always enjoyed an enviable reputation and for obvious reasons, it is with deep regret that the occasion makes such a report necessary, but in view of all the evidence presented, such a finding is, in the Court's opinion, inescapable.

"The Court would like, at this time to commend the fair and remarkably able presentation of the evidence to the court by _____, the Assistant District Attorney for the County of _____, representing the Commonwealth. The Court would also like to commend the Police Department, and Sgt. _____ of the _____ State Police attached to the District Attorney's Office for the County of _____ for their competent and thorough investigation of the matter."

Also of serious import is the *civil* liability of the hospital, the trustees, the administrator and the pharmacist in negligence suits arising from injuries or deaths where a nonprofessional (Pharmacy Helper or Ward Attendant) acts in the capacity of a licensed pharmacist with the consent, expressed or implied, of the hospital. I shall speak more about this under the subject of need for insurance for pharmacy practitioners in hospitals.

Pharmacy vs Nursing Acts

I have been asked many times by hospital administrators, hospital pharmacists, nurses, Department of Public Health and State Board members and inspectors in the United States the differences, if any, between "drug dispensing" (a pharmacist act) and "drug administration" (a nursing act).

In this connection, I would point out at the outset that United States law is a complex specialty made so because of the existence of a set of Federal Laws, 49 sets of State Laws and many county and municipal laws and regulations. *Here and elsewhere in this presentation, we can only hope to discuss law principles in general or the law applied to a particular fact situation in a given State. When specific legal problems arise, one must consult the local law and this can only be done intelligently through an attorney, competent in that local law.*

Now to the issue of "drug dispensing" and "drug administration." Each state must have, as I see it, as safe a practice of pharmacy for its hospitals, clinics, nursing homes and rest homes as it has for its drug stores or shops, its community practitioners of pharmacy. Two points I would emphasize—pharmacy helpers, ward attendants, and others must know and understand that they work *only under the direct and immediate supervision of pharmacists* if they assist in pharmacy activities and secondly, hospital authorities must be careful not to assign to nursing duties these acts purely pharmaceutical in nature.

Drug Dispensing vs Drug Administration

Drug Dispensing, in my opinion, is a function that is by custom, tradition and law, restricted to licensed practitioners of pharmacy in the United States. It is distinguished from *drug administration,* an act associated with the practice of nursing, in that *drug dispensing* involves (1) the issuance of one or more doses of a medication in containers other than the original, such new containers being properly labeled by the dispenser as to contents and/or directions for use as indicated by the prescriber *or* (2) drug dispensing is the issuance of a medication in its original container with a pharmacy prepared label that carries to the patient the *signa* of the prescriber as well as other vital information *or* the package carries a label prepared for nursing station use in a hospital. The contents of the container may be for one patient (such as an individual prescription) or for several patients (such as a nursing station medication container).

Drug Administration

In *drug administration,* a nursing act, a single dose is administered to a patient by the nurse as a result of an order of a physician or dentist. Should a pharmacist, for example, prepare a prescription or medication order of a radio-active medication for a particular patient and also administer this medication to that patient, that pharmacist is in violation of the Nursing Practice Act. He is criminally liable as well as would be the hospital that would allow this practice to continue. In hospital practice, to avoid charges of violation of the Pharmacy Practice Act, of the several states, one must be careful to discern between drug dispensing and drug administration. The removal from the Pharmacy to the nursing station of a single dose of a drug from the original container by a nurse for a specific patient or the removal from the Pharmacy to the nursing station of a pharmacy prepackaged and properly labeled nursing station medication container by a nurse falls under "drug administration" and is legal. However, the filling or refilling of a nursing station medication container with the drug called for is *"dispensing"* and can be engaged in legally *only* by a licensed pharmacist, under the Pharmacy Practice Act of the state. Also, it can be argued that the removal of the original container from the storeroom or Pharmacy to a nursing station is "drug administration" as well as "Drug Dispensing" and is both a legal pharmacy and nursing act, though not a very practical one. Note that *no* transfer from container to container occurs *nor* is there a possibility of label error. *The public health point at issue revolves around patient safety and error control. Should a nurse remove the single dose from the wrong container while at the Pharmacy (drug administration), there is no greater liability involved than the doing of the same act at a nursing station.* However, the filling of a nursing station medication container falls into the Pharmacy Act of "dispensing" in that an error here could injure all patients who subsequently receive medication from that container. Because of the seriousness of this pharmacy practice violation in hospitals and nursing homes in many states, it is imperative, we believe, that individual State Boards, Departments of Health, and State Hospital, Nursing Home and Pharmaceutical Associations in the United States take the necessary action to clarify who in State Government shall enforce the Pharmacy Practice Act and drug control activities in hospitals and further, see to it that such codes and regulations are enforced.

Degree of Skill and Care Required of the Hospital Pharmacist

In a leading case (Tombari *vs.* Connors 85 Conn. 231, 1912) the pharmacist filled a prescription calling for Calumba gr. v. per powder with Calomel (Mercurous Chloride). Calumba was prescribed in *1912* as a simple bitter. Its dose was up to 30 grs., 3 or 4 times a day. Calomel, a cathartic, was usually prescribed in ¼ gr. doses every 15 minutes until 2½ grs.

had been taken (10 doses). The Court found that:

"ordinary care with reference to the business of a druggist must therefore be held to signify the highest practicable degree of prudence, thoughtfulness, and vigilance and the most exact and reliable safeguards consistent with the reasonable conduct of the business in order that human life may not constantly be exposed to the danger flowing from the substitution of deadly poisons for harmless medicine."

Therefore, while the degree of skill and knowledge of a hospital pharmacist is much higher than that expected of a lay person, it need be no higher legally than the skill and learning possessed by the average hospital pharmacist in the same area or state.

Manslaughter

A case involving a charge of criminal negligence has already been discussed (Judge Mayberry's Inquest Report). May a pharmacist be held for manslaughter in the event of a death in the improper compounding and dispensing of a medication? In People *vs.* Stuart, 302 P. (2d) 5 (Calif. Oct. 1956) the pharmacist filling a prescription for Sodium Phenobarbital, grs. eight; Sodium Citrate, drams three; Simple Syrup, ounces two; Aqua Peppermint, ounces one and Aqua Distillata Q.S. Ad ounces four, dispensed 3 drams of a powder from a bottle labeled Sodium Citrate. The material dispensed from the bottle was found to be Sodium Citrate and *Sodium Nitrite.* As a result, the patient, a child aged eight, died.

In the lower court and the District Court of Appeals the pharmacist was convicted of manslaughter. However, the California Supreme Court stated that in order to be guilty of manslaughter, a criminal intent must be shown. If, continued the Court, the person who committed the act or made the omission charged was acting under ignorance, or mistake of fact, he has *no criminal intent* and is incapable of criminal negligence. This is also true, the Court stated, of persons who commit an act through misfortune or by accident, when there appears that there was no evil design, intention or culpable negligence. The judgment or conviction was reversed by this Court holding that the defendant acted with due care and caution and not ignorantly. The Court further stated that the defendant had the right to rely upon the fact that the bottle marked Sodium Citrate did, in fact, contain Sodium Citrate and not something else.

In Oklahoma in late 1955 or 1956, a pharmacist was charged with dispensing Potassium Cyanide for Potassium Citrate to the extent that 10 percent of the prescription contained the poison. Damages totaling $62,893 were awarded in a Civil Tort action in a District Jury Court for the death of a woman who took the prescription. In addition, the pharmacist involved was charged with manslaughter. I have no information as to the final outcome of the case in my records.

Parenthetically, I might mention that Common Law manslaughter in the United States is usually defined as a homicide committed without justification or excuse and without malice. *Voluntary manslaughter* is homicide in heat of passion caused by provocation reasonably exciting passion, such as assault or killing in mutual combat. *Involuntary manslaughter* is homicide that results from the doing of an unlawful act, not amounting to a felony, and not of such a nature as to cause a reasonable apprehension of causing death, or where it results from reckless or wanton acts. Common law manslaughter in Maryland, for example, is a felony and carries a 10 year maximum sentence, while statutory manslaughter such as manslaughter by automobile is a misdemeanor and carries a three year sentence. In the California case, *pharmaceutical manslaughter* as well as Common law manslaughter was carried in the indictment. The defendant's attorney in arguing the case before the California Supreme Court won his reversal of a conviction of manslaughter by a lower court by arguing that pharmacy is a profession not unlike medicine or law. He argued, "A pharmacist can no more be guilty of manslaughter if an error (without intent or negligence) results in death, than can a District Attorney or Judge in a lower court be held for false imprisonment after a higher court has reversed a conviction." The District Attorney had based his case on the theory (1) that the pharmacist was the *absolute* insurer of what he delivered and if anyone died as a result of a prescription, he was guilty of manslaughter, and (2) that selling an admittedly adulterated drug which resulted in a death was an unlawful act and hence the pharmacist was subject to a charge of manslaughter under California laws. In the Appellate Court, a reversal of the *pharmaceutical manslaughter* conviction was obtained and in the Supreme Court the manslaughter charge conviction of the lower court and upheld by the Appellate Court was reversed.

Minimum Standards

In an effort to provide better care of patients in hospitals, those responsible for hospital care have sought and fought for better standards, laws and regulations.

Let us now consider the hospital, the trustees, administrators, and hospital pharmacists in connection with their legal responsibilities in connection with these standards, laws and regulations. This is a serious problem today in the United States—one being discussed by lawyers that are specialists in hospital jurisprudence. One must today, in the United States, take cognizance of the prevailing rules of evidence in the courts and their effect on the admission into court of standards, laws, regulations, medical records and manuals. I refer in particular to the rules re-

garding hearsay, and the *Res Gastae* (the spontaneous declaration or act which grew out of or is part of main fact), and the *Res Ipsa Loquitor* (this thing speaks for itself). Hearsay evidence is, as you know, the statements of a party made outside of a court, not by a party to the suit and not under oath. Hearsay, as a general rule, is not admissable as evidence. For example, Mass. C.L. Ch, 233, Sec. 79 reads, "Hospital records of hospitals supported in whole or in part by the public or public contributions *are* admissible as evidence and are not excluded under the hearsay rule." However, because Massachusetts is one of the states in the United States still operating under the charitable trust doctrine, anything touching on the issue of this type of liability (negligence) *cannot* be read or introduced in a suit in that state against a hospital. This statute allows only the original record to be admitted and not copies. The same would no doubt hold true for standards, laws, and regulations. One must check the case law (*Stare Decisis* Doctrine) and statutes in one's own state to determine the admissibility of these items as evidence.

Procedure Manuals

To these laws, statutes, regulations, and standards, I should now like to introduce one of the contemporary innovations of hospital management—procedure and policy manuals, manuals of operation for the different departments of the hospital such as for the nursing service, the dietetic service, the pharmaceutical service and others.

What is the legal status of procedure manuals? In Massachusetts, such manuals would constitute valid evidence in negligent cases involving other than the doctrine of charitable immunity. The first key as to the direction a court will take hinges on the extent of the charitable immunity doctrine of the state in reference to hospital suits. In certain states with well relaxed charitable immunity doctrines, such manuals could be introduced as evidence to prove rules of conduct or safety promulgated by the hospital. When such rules are violated and negligence ensues, what better way to show violation of rules than by a recital of the manual's contents on the point at issue, if such evidence can be admitted?

What am I leading to? Simply this. That principles and standards laid down to guide: the laws, their regulations, minimum standards, procedural manuals, and the like become, in time, tools to be used in law work in applying the degree of standard or the degree of care, *below which,* a hospital might conceivably be found guilty of negligence. Established standards for pharmaceutical services in hospitals, once accepted as standard operations holding to the "reasonable test" in law, give the courts cause to accept such standards in determining what is reasonable to expect as to the competency of an average pharmacist or pharmaceutical service in a hospital. Therefore, new and improved standards in nursing, surgery, pharmacy, and other areas throughout the hospital which yield better patient care bring with them recognition of these standards by the courts as a sort of *modus operandi* and are accepted. Failure to meet these minimum requirements might mean taking the possible legal consequences of having evidence submitted tending to substantiate the negligence claim.

One court in the United States has already mentioned "written rules" for the conduct of a hospital pharmacy and "standard practice" procedure—the Connecticut Boric Acid-Dextrose case mentioned previously. On appeal, the court stated: "All of the evidence was to the effect that the pharmacy was set up in accordance with standard practice, and there was no evidence to the contrary. *No* written rules for its conduct had been prescribed and there was no evidence that standard practice required this or that their existence would have changed the situation."

Furthermore, in litigation, the hospital records may be brought into court by *Subpoena Duces Tecum.* In pharmacy, this could mean the procedural manual, the formulary, prescriptions, and the minutes of the Pharmacy Committee meetings as well as the components of the patient's medical record.

The modern up-to-date hospital, I believe, must keep live files of pertinent laws, regulations, standards, and procedures. Quite conceivably a hospital in the United States not meeting today's standards for its hospital pharmacy as judged by the requirements of the Joint Commission on the Accreditation of Hospitals and the Minimum Standard for Pharmacies of the American Society of Hospital Pharmacists might be charged with negligence in operation. Negligence, as here used, refers to the *not* doing of something that a reasonably prudent man should do, or the doing of something that a reasonably prudent man would not do, with resulting injuries to another. It is essential then, for responsible hospital officials including Chiefs of Pharmaceutical Services to review critically and frequently the operations of their pharmaceutical services and pharmacy intern programs in the light of Federal, state, and local hospital, Public Health, Food and Drug, and pharmacy statutes and regulations; the Minimum Standard for Pharmacies in Hospitals of the American Pharmaceutical Association and the American Society of Hospital Pharmacists, and the accreditation program of the Joint Commission on Accreditation of Hospitals. Procedures should also be checked against the hospital's procedural manual. Then, at least the administrator and chief pharmacist will know of weaknesses and take corrective measures in the interest of better patient care and for protection of the hospital and themselves against law suits.

Prescription Writing, Signa

Hospital administrators and hospital pharmacists, physicians, and dentists should be aware of the legal responsibilities that affixes to the hospital and themselves where an employee-physician, or employee-dentist prescribes a medication with a "use as directed" signa or with oral directions. Should a patient fail to follow the physician's oral directions or misunderstand a "use as directed" instruction on a prescription label and, as a result, injures himself with the medication, the physician or dentist is and the hospital may be held liable. All that is necessary is for the plaintiff to prove that a failure to write a clear signa constitutes negligence. In a Kansas case, a patient was orally instructed to take one teaspoonful of the prescribed drug every four hours. The patient misunderstood the directions and took four teaspoonfuls every hour. The jury awarded $10,000 damages against the physician.

Age on Prescriptions

Where an overdose is clearly noted on the prescription by reason of age, the hospital, the physician, and the pharmacist may be held jointly liable. However, if the age of the patient is left off the prescription, and the patient's age is material, the hospital, if the physician is an employee of the hospital, and the physician may well be liable.

Liability of Hospital for Acts of Hospital Pharmacists

Should a specific P.R.N. order, or standing order, be in question before the Court, its proper life would be based on the law of reasonableness based on expert testimony. From our knowledge of tort law and negligence, each person (here, the nurse) is generally liable for any acts of his which cause injury to another. We also know that the legal maxim *Que Facit Per Allum, Facit Per Se* (he who does through another, does himself) applies when the individual, in the employ of another and in the normal course of duty, injures a third party. In such cases, the employer is liable for the employee's acts. So, in accordance with the master-servant (respondent-superior theory) or principal-agent relationship, the hospital is liable for the wrongs of its employees.

Principles similar to those described under the P.R.N. order apply to the hospital pharmacist in filling prescriptions, house orders, and other requests. However, note that I qualified the liability of the hospital in the United States with a "may be liable" statement. While a master or principal is normally liable for the acts of his agents and servants in the performance of their prescribed duties (but not on "frolics of their own"), this negligence of an employee cannot be charged to the hospital employer in some states unless he can be charged with a lack of due diligence and care in the selection of the employee or, as in Massachusetts, under no condition can the hospital be held liable under its strict Charitable Trust Immunity Doctrine.

Elements Necessary to Establish Negligence in Tort Cases

Let us next consider the common law as applied to compounding and dispensing in the hospital pharmacy. I suspect United States law is little different than French or English law in this area. In establishing negligence in a tort case, three elements must be proven in the United States:

1. A legal duty to exercise care;
2. Evidence that this duty has not been exercised; and
3. An injury resulting from the non-exercise of this duty.

In drug compounding or manufacturing in hospital pharmacies and elsewhere the lack of exercise of the legal duty to exercise care might be any one or more of the following acts:

1. Improper formulation, such as a "gas producer;"
2. Inadequate testing and inspection of raw materials and/or the finished product;
3. Failure to warn by label against *improper use* of known dangerous properties of the product or failure to sufficiently warn of the dangers involved in use of the product as, for example, the *lethal* danger in inhaling carbon tetrachloride vapors, (Texas case), and "that certain persons are allergic to the drug" such as Aluminum Sulfate (*Consumer Bulletin,* July 1958);
4. Carelessness in compounding or bulk compounding resulting in an unsatisfactory, harmful or filthy product being released to the public.

Defences Against Negligence

When an error and injury are shown, a presumption of negligence exists. The hospital or pharmacist to prove non-negligence, may avail himself of one or more of the following defenses:

1. Prove he used proper care;
2. Prove contributory negligence (reliance on knowledge and skill of pharmacist is not considered contributory negligence—Wilcox *vs.* Butt's Drug Stores, 38 New Mexico 502, 1934).
3. Prove that the real or proximate cause of the injury was not directly due to his negligent act (exception to this is the cases of items "inherently dangerous"—see Thomas vs. Winchester case below).

Thomas *vs.* Winchester, 6 N.Y. 397 (1852), is often quoted as the leading United States drug case on the liability of an individual to a third person

when items inherently dangerous are involved. In brief, the placing in motion of a harmful agent, such as the selling of a poison (Tincture of Belladonna) carelessly labeled as a harmless medicine (Extract Taraxacum-Dandelion), places the person responsible for such issuances legally liable to all persons injured through no fault of their own in consequences of the act: (See also leading Squid case—Scott *vs.* Sheppard, 2 Wm. Blackstone 892). Such cases are brought into court on tort grounds based on negligence—negligence in the delivering of goods that are inherently or imminently dangerous. "One releasing a wild lion or tiger on society is responsible for its acts." This law stems from the belief that the original act of delivering or releasing such an article is wrongful. The hospital is brought into such suits, on the grounds of negligence of its employee—the master-servant doctrine of principal-agent theory carrying over the liability to the employer.

Contract Law

The theory of *Caveat Emptor* (let the buyer beware) of the Law of Sales on the contact side, does not normally apply to the sale of drugs and medications. This legal doctrine is based on the premise that the average person is not skilled or informed on this subject and therefore must rely on the pharmacist vender to furnish the item called for (Jones *vs.* George, 36 Texas 149 (1882), Tombari *vs.* Connors, 85 Conn. 231 (1912), Mann-Tankersly Drug Co. *vs.* Cheairs & Sons, 75 Ark. 596 (1905). The theory of *Caveat Vendor* (let the seller beware) prevails, not *Caveat Emptor* (let the buyer beware) in such a situation. Also, the doctrine of *Res Ipsa Loquitor* (the thing speaks for itself) and *Res Gestae* (a spontaneous declaration simultaneous to the act and therefore a part of it), may be applied, *i.e.* there is a presumption of negligence if one is injured as a result of overdose or improper filling of prescriptions or improper manufacturing or bulk compounding.

Elements Necessary to Prove Breach of Contract in Contract or Sales Law

When a pharmacist fills a prescription, all the normal rules of contract law apply plus certain implied warranties from the law of sales. The pharmacist impliedly warrants in each prescription he fills that:

1. He has the skill of an ordinary pharmacist;
2. He used due and proper care in filling the prescription;
3. He used all proper ingredients—did not substitute; and
4. He used no other ingredients, other than those properly allowed under reasonable *"misce secundum artem"* principles.

A breach of warranty applies normally only to parties in privity in contract, not to third parties. An exception exists in food and medication cases. However, it is sometimes easier to prove a case of this type as previously stated, through negligence suits on the tort side of law. Therefore, parties in privity often times make use of the tort side of law rather than contract in negligence actions although either type of action is available to them.

Absolute Liability Doctrine

See Escola *vs.* Coca Cola Bottling Co., 24 Cal. 2d 453. This doctrine is used in a limited fashion in the United States. The California Judge in the Coca Cola case cited above stated:

"In my opinion, it should now be recognized that a manufacturer incurs an *absolute liability* when an article that he has placed on the market, knowing that it is to be used without inspection, proves to have a defect that causes injury to human beings. Even if there is no negligence, *public policy* demands that responsibility be fixed wherever it will most effectively reduce hazards to life and health inherent in defective products that reach the markets. It is to the public interest to discourage the marketing of products having defects that are a menace to the public. If such products nevertheless find their way into the market, it is to the public interest to place the responsibility for whatever injury they may cause upon the manufacturer who, even if he is not negligent, is responsible for its reaching the market. However, intermittently such injuries may occur and however haphazardly they may strike, the risk of the occurrence is a constant risk and a general one. Against such a risk, there should be a general and constant protection and the manufacturer is best situated to afford such protection."

The Cutter Polio Case

I promised to speak to the "implied warranty" doctrine as applied to the recent Cutter polio case. As I have previously indicated, it is well established in the United States in our "Law of Sales" that the legal principle of *Caveat Emptor* (let the buyer beware) does not apply in the sale of food and medications but rather the principle of *Caveat Vendor* is invoked. In the sale of food and medication there exists an implied warranty of fitness for use and an implied warranty of merchantability. This is not new law in the states of the United States. It has, for many years, been law that items such as food and medications carry this implied warranty of fitness for use and therefore manufacturers and vendors of such items are liable for damages in the event injury results from the use of the goods. The unusual point in the Cutter case is the extension of the doctrine to situa-

tions where the manufacturer is in *no* degree negligent as in the manufacture of a truly new medication. The law in the polio case simply stated runs as follows: If a product is made according to the highest attainable known standards of strength, quality and purity, and is adequately labeled for professional use, the implied warranty of fitness for use principle will be applied if injury results to the user, *even though nothing was known prior to the incident that such an adverse reaction could occur. In other words, the manufacturer and vendor are liable.*

It has long been law in the United States that where the buyer, expressly or by implication, makes known to the seller the particular purposes for which the goods are required, and it appears that the buyer relies on the seller's skill or judgment, whether he be the grower or manufacturer or not, there is an implied warranty that the goods shall be reasonably fit for such purposes. The two prerequisites for this implied warranty of fitness for use are:

1. The buyer makes known to the seller the particular purpose for which the goods is required; and
2. The buyer relies upon the seller's skill and judgment.

Farrell *vs.* Manhattan Market 198 Mass. 271.

One exception to this usual test has prevailed—in the case of the sale of a specified article asked for *by its patent or trade name* (not if trade name is requested by the buyer by other than trade name—Warren *vs.* Shulte, 275 Mass. 379), there is no implied warranty as to its fitness for any particular use. However, even in such instances, while the implied warranty for fitness may not be present, another implied warranty exists, and may be applied—the implied warranty of merchantability. This warranty applies where goods are bought from a seller who deals in goods of that description whether he be the grower or manufacturer or not. Further, the item need not be for resale purposes nor be bought by "description." (Botti *vs.* Canice Grocery Co., 35 N.E. (2) 491 (1941). ("LaRosa Macaroni" sold to consumer).

It will be noted that when one sues in tort on the grounds of negligence, one must prove the defendant knew of his negligence or should, as a reasonable man, have known of his negligence. In suit on a sales contract one need *not* prove negligence to prove a breach of an implied warranty, such as fitness for use or merchantability.

The Cutter decisions (Gotts Danker *vs.* Cutter Laboratories, Inc. and Phipps *vs.* Cutter Laboratories Inc. [Calif.] January 1958) are an extension of this sales law of product liability to these situations where nothing was known prior to the incident that such serious adverse reaction could occur.

In the past, the risk inherent at this point in the development of *new* medications has been one assumed by the individual users providing no negligence was attributed to the maker. The Cutter decision, if not overruled in the California Appellate Court, transfers this risk to the maker of the new medication. Attorneys for drug associations and firms in the United States have voiced the fear that the Doctrines of Implied Warranty of fitness for use or merchantable as applied in the Cutter case, may slow down the introduction and marketing of new drug products.

Dr. Albert Holland, Jr., Medical Director, United States Food and Drug Administration, stated recently, "in view of some recent court decision on the Doctrine of Implied Warranty, placing a new drug on the market becomes an increasingly important management decision. To be first remains of tremendous importance, but it does not take more than one major product mishap to demonstrate the wisdom of the old saying 'It is better to be safe than sorry.' In view of the development of high potency drugs, the theme will be toward longer periods of investigative study with larger series of patients and in the hands of more clinical investigators."

In years past, privity of contract had to be established in such warranty cases. However, in recent years, this privity of contract doctrine has been abandoned in food cases due to the nation's shift in social philosophy. Today, the law in some states imposes these implied warranties upon the manufacturer and seller of food products without privity of contract between the ultimate consumer and the seller or the manufacturer (Klien *vs.* Dutchess Sandwich Co., Ltd. 14 Cal. 2d (272) (1939)). In the California Cutter situation, the rule was further extended to manufacturers of pharmaceutical products. However, in some states the courts still require privity in warranty actions and where lacking with the manufacturer recovery is denied on the warrant principle (Spencer *vs.* Cutter Laboratories (Tenn.) (1956)).

Several safeguards have been mentioned in the American literature as to legal means available to protect drug manufacturers from this decision, especially as it relates to the introduction and marketing of new drug products. For example, the use of an extended type of product liability insurance and the use of the disclaimer clause have been advocated. *Another possibility that needs to be explored is a Federal program of compensation similar to that used by labor and industry for industrial accidents—the application of the principles of the Federal Workmen's Compensation Act.* This possibility appears to have sound public policy and public good implications.*

Applying the Cutter case principle to hospital pharmacy practice, we note that when the patient receives

*See Author's Note, page 116.

the product through his hospital, a charge may be and is usually made for the product. It is conceivable under such circumstances that the hospital becomes a seller within the meaning of the Uniform Sales Act and thereby warrants to the patient in accordance with the rules of the Cutter case, however this liability of such intermediate parties in many instances *may* be referred back to the manufacturer (Royal Paper Box Co. *vs.* Munroe and Church Co., 284 Mass. 446.)

Insurance

Hospitals normally carry, in addition to others, three types of insurance peculiar to their type of operation: Hospital Professional Liability Insurance; Public Liability Insurance; and Products Liability. Hospital Professional Liability Insurance covers claims of patients against malpractice claims of employees in diagnosis and treatment. This policy usually covers** the furnishing or dispensing of drugs to inpatients and to outpatients and also prescription refills. This is a coverage that should be carefully checked by each hospital pharmacist and administrator.

Public Liability Insurance deals with claims arising out of accidents because of plant defects, temporary or permanent, such as falling on steps, etc. This type of insurance is of little concern in this discussion. Lastly, Products Liability Insurance is a type of protection provided against claims arising from the consumption of products manufactured, sold, handled, or distributed by the hospital for inpatient or outpatient use. This type of policy is of particular value where the hospital operates a coffee shop, tearoom or drug store open to the public. An example is the sale of hospital pharmacy-made cold cream to general public. This insurance policy also should be carefully checked and made to cover products of the pharmacy department, as well as the usual drug store items.

At this point, it seems proper to mention that hospital pharmacists as well as physicians and nurses in the United States are giving serious consideration to covering themselves *personally* with Professional Liability Insurance. The cost is negligible and the protection great. Too often hospital pharmacists in the United States assume that their hospital employer's malpractice insurance covers them personally. This is seldom the case. Cost of such protection in the United States varies from state to state. However, a $25,000/$75,000 policy usually costs under $20.00.

Prescriptions As Privileged Communications

Certain information contained in the medical records is privileged in the United States, that is, having been obtained as a result of a confidential relationship between the parties; the recipient of such information cannot be legally compelled to disclose this information. Prescriptions *may* belong in this classification. This is a matter for the hospital's attorney to decide, based upon the facts in the case, the prescription itself, and the law of the particular state. Some states (New York and Mississippi) have indicated that physician's prescriptions are not considered "privileged" after they have been submitted to the pharmacist (133 NYS 2d 27 in re: Niver's Will, also 84 NYS 887, and 66M 588). A *Subpoena Duces Tecum* is used to produce the prescription in court.

Destruction of Prescriptions

Destruction of a prescription may be used as evidence admitting guilt (Marigny *vs.* DeJoie La. 1937 172 80 808). Therefore, all prescriptions should be preserved the full period of the Statute of Limitations of the state. Further, under the "best evidence rule," the highest degree of proof should be available, in this instance, the original written prescriptions (see below for legal time requirements of holding).

Ownership of the Prescription

State and Federal Codes and Statutes must be applied in this instance. However, in general, it may be said that the prescription is the property of the patient until filled—then, because it falls under the best evidence rule and for other reasons, it belongs to the pharmacy or hospital.

By statutes and codes today, many prescriptions are not refillable and the pharmacist or hospital must account for stocks of such items. Narcotics, hypnotics, and "Prescription Legend Drugs" are in this category. Obviously, the filling of such prescriptions implies as part of the contract of sale the keeping of the prescriptions by the pharmacy.

Length of Time to Hold Filled Prescriptions

Narcotic prescriptions—Federal Harrison Narcotic Act—2 years; Prescription Legend Drug Prescriptions - Federal Food, Drug, and Cosmetic Act—3 years; Ethyl Alcohol records, etc.—5 years. *All* prescriptions—x number of years - the number of years depending upon the pharmacy laws and the Statute of Limitations for a tort claim in the particular State in question. (Federal —A tort claim against the United States shall be forever barred unless action is begun within two [2] years after such claim accrues. Chapter 92, Public Law 55 - 81 Congress - 1949 - 28 U.S.C.A. 2401b).

*Author's Note: *Drug Trade News,* December 29, 1958, reports that the National Drug Trade Conference's Executive Committee will soon consider the feasibility of state or federal legislation designed to limit liability of pharmaceutical manufacturers for injuries resulting from the use of their products by consumers. *American Druggist,* December 15, 1958, page 20, reports on suggestions of attorney that U.S. share liability risk regarding "Crash Program" Drugs. Attorney points to 1957 amendment to the Atomic Energy Act as a clear pattern for the development of an "Effective Risk —Spreading Device" in the drug field in order to minimize the liability of individual manufacturers.

**Manual on Insurance for Hospitals, American Hospital Association (1955).

Investigational Drugs

A word about new or investigational drugs is in order. These are drugs that are not as yet available in interstate commerce in the United States. Section 201(p) of the Federal Food and Drug Act defines a "new" drug. Before a manufacturer may release a new drug, it is submitted to the New Drug Section of the Food and Drug Administration with "full reports of all investigations made to show whether or not such drug is safe for use."

New drugs before release in interstate commerce, and while in clinical trial, are labeled, "Caution—New Drug - Limited by Federal Law to investigational use." Such drugs may be used only by *experts* of drugs. Obviously, this work must be done by individuals with qualifications in excess of those ordinarily possessed by practicing physicians and dentists. Such individuals must be experts on the *safety* of drugs. Again, the law of reasonableness is applied to determine whether a certain physician is an "expert" under this statute. In other words, would a reasonable and prudent man, after viewing the formal training and/or experience of the particular physician, consider that he is an expert on the safety of the particular class of drugs under study?

Approval or rejection of a new drug application must be made by the Government within sixty days of application. If negative action has not been taken within the sixty day period, the application becomes effective. This section of the law was not in existence at the time of the sulfanilamide elixir incident that resulted in the death of over 100 persons many years ago.

The *Statement of Principles* issued by the American Hospital Association on the use of investigational drugs again illustrates my point on standards and the law. Should an injury occur to a patient in a hospital by the use of an investigational drug and these American Hospital Association Principles were not followed, the plaintiff attorney would be furnished with a good tool to attempt to impute negligence to the hospital, the clinician, trustees and others involved.

> Statement of Principles Involved in the Use of Investigational Drugs in Hospitals Approved by Board of Trustees of the American Hospital Association - September 29, 1957

Hospitals are the primary centers for clinical investigations on new drugs. By definition these are drugs which have not yet been released by the Federal Food and Drug Administration for general use.

Since investigational drugs have not been certified as being for general use and have not been cleared for sale in interstate commerce by the Federal Food and Drug Administration, hospitals and their medical staffs have an obligation to their patients to see that proper procedures for their use are established.

Procedures for the control of investigational drugs should be based upon the following principles.

1. Investigational drugs should be used only under the direct supervision of the principal investigator who should be a member of the medical staff and who should assume the burden of securing the necessary consent from the patient.
2. The hospital should do all in its power to foster research consistent with adequate safeguard for the patient.
3. When nurses are called upon to administer investigational drugs, they should have available to them basic information concerning such drugs - including dosage forms, strengths available, actions and uses, side effects, and symptoms of toxicity, etc.
4. The hospital should establish, preferably through its Pharmacy and Therapeutics Committee, a central unit where essential information on investigational drugs is maintained and whence it may be made available to authorized personnel
5. The Pharmacy Department is the appropriate area for the storage of investigational drugs, as it is for all other drugs. This will also provide for the proper labeling and dispensing in accord with the investigator's written orders.

Compounding Pharmaceuticals Covered by Patent

The Minimum Standard for Pharmacies in Hospitals in the United States quite naturally, advocates the use of *U.S.P., N.F., N.N.D.,* and *A.D.R.* drugs and preparations. These texts contain, among others, preparations covered by patents and trade marks. The *U.S.P.* carries, as you know, this statement: "Notice and warning. Concerning Patent and Trademark Rights—The inclusion in this Pharmacopeia of any drug in respect to which patent or trademark rights may exist shall not be deemed, and is not intended as, a grant of, or authority to exercise, any right or privilege protected by such patent or trademark. All such rights and privileges are vested in the patent or trademark owner, and no other person may exercise the same without express permission, authority, or license secured from such patent or trademark owner." The *N.F.* carries a similar statement.

Hospital pharmacists engage both in actual compounding and dispensing activities. In the course of their official duties, hospital pharmacists receive prescriptions or house orders for ointments, creams, lotions, collyria, and other forms of medications. These may they elect to purchase or to compound, depending upon the economics involved.

Should a prescription or order be received for an item in a *use form* that is covered by a patent right, whether it be in an official compendium or not, the pharmacist in the United States *cannot* legally compound or manufacture the item, unless he or the hospital has obtained a license or permission from the holder of the patent, to engage in the compounding or manufacture of the preparation.

An interesting point in this connection is that patents may be taken out under the Patent Act based on a "new use." Title 35 (section 100(b)) provides that

"the term 'process' means process, art or method and includes a new use of a known process, machine, manufacture, composition of matter or material."

To illustrate the point, *The Bulletin of The American Society of Hospital Pharmacists* carried in its October 1951 issue, an article on "Chlorophyll, Its Medical and Pharmaceutical Applications." In January 1952, the holders of the patent rights (United States Patent Office, 2,120,667.) covering the therapeutic use of water-soluble chlorophyll had this to say in an open letter to the Editor, which was published in the same publication: "We feel that this article has created a situation which can damage our company considerably and can conceivably cause hospital pharmacists and others to think they can manufacture these chlorophyll preparations without violating our patents."

Incidentally, this manufacturer brought suit against another drug company in the Texas Federal Court (Northern District) charging infringement of patent by producing ointments, solutions, and tablets of chlorophyll. It was awarded $6,727 in damages with the defendant becoming a licensee of the patent holder.

Not to belabor the point further, but to indicate the feeling of the Federal Veterans Administration on this subject—in April 1952, a release to Veterans Administration hospitals signed by the Chief Medical Officer, restricted all pharmaceutical services of the Veterans Administration from engaging in the manufacture of "patent pharmaceutical preparations."

Summary

In conclusion, let me summarize the legal responsibility of the hospital pharmacist in the United States. The hospital pharmacist is liable for his own acts of negligence. He is also liable for acts of those under his supervision when their acts are in the performance of their duties. As a pharmacist, he is licensed by his state to practice his profession. His hospital, unless a strict charitable trust immunity doctrine prevails in the state, is also responsible for his acts and the acts of his subordinates through the respondent superior principle. His administrator and hospital may tell him "where" and "when" to practice his profession, but never "how" to practice. This "how" is the practice of pharmacy for which the state has licensed the individual, not the hospital, not the administrator, nor the Board of Trustees. To avoid liability toward his hospital and himself, the hospital pharmacist must refuse to do certain acts or refuse to allow them to be done by his staff when he knows the acts are not proper or legal to his profession. He cannot in defense claim he was ordered by the administrator of the hospital to do acts outside the law such as the utilization of non-pharmacists or nurses in compounding and dispensing activities.

To protect himself, the hospital pharmacist should carry malpractice insurance and to protect his hospital he should urge that it too carry product liability and malpractice insurance on activities of his department. To further protect himself and his hospital, Wm. A. Regan, a noted attorney on hospital law in the United States in a paper recently published in the *Modern Hospital* states:

"(1) We recommend the formulation of a *written* administrative policy with reference to the operation of the hospital pharmacy." By this Mr. Regan no doubt means the policy and procedure manual previously discussed. Among other things, the manual might well cover an automatic stop order policy, provisions for legal pharmaceutical service in off-pharmacy hours, hospital policy on P.R.N. and standing orders, and adequate controls on narcotics, hypnotics, restricted drugs, bulk compounding and prepackaging operations, as well as hospital policy on the use of generic names in prescribing and labeling; the hospital formulary system and the function, duties and responsibilities of the Pharmacy and Drug Therapeutics Committee.

"(2) We recommend *Central Control* over the total pharmacy function in the general hospital." This would no doubt cover the extension of the use of the pharmacist to cover supervision of drugs, chemicals and housekeeping cleansing agents found at nursing station medication centers and at janitor's supply quarters or closets, as recently recommended by the American Hospital Association.

"(3) We recommend special emphasis upon adequate storage facility and segregation of poisonous and nonpoisonous pharmaceuticals, narcotics and medications.

"(4) We recommend the practice of preparing short, specific *written memoranda* from the hospital pharmacist to the designated administrative officer regarding any inherently dangerous situations in pharmacy which, in the opinion of the hospital pharmacist, might lead to some accident or untoward happening resulting in injury to a patient." This last point is indeed a vital one for it gives positive knowledge to all concerned of serious defects that from a legal point of view peril the Chief of the Pharmaceutical Service, the administrator and the hospital trustees, as well as patient care and safety.

To speak to you here in Brussels on these broad general principles of common and statutory law has been a delightful experience. Time has not permitted any discussion of the Federal, state and local codes or statutes such as narcotic, hypnotic, ethyl alcohol, marihuana, etc, that apply to hospital pharmacy in the United States. Further, time has not allowed for a legal discussion of fair trade, over-the-counter, or product duplication, imitation and substitution problems in the U. S. Should you have any questions in these areas, I shall do my best to answer them. I trust I have been helpful. Thank you.

a program for
RECEIVING MEDICAL SERVICE REPRESENTATIVES
on a monthly basis

by HERBERT L. FLACK

► THE FOLLOWING PROGRAM IS THE ONE IN use at Jefferson Medical College Hospital for receiving medical service representatives in the Pharmacy on a monthly basis. This procedure is followed for representatives of pharmaceutical and surgical supply companies. It is presented here in the belief that it may be of interest to other hospital pharmacists.

PHARMACY SERVICE
JEFFERSON MEDICAL COLLEGE HOSPITAL
PHILADELPHIA 7, PA.
December, 1958

Pharmaceutical and Medical and Surgical Supply Company Representatives

In keeping with the policy of being "detailed" once monthly, this is to advise of the dates and responsibilities anticipated during the year 1959.

Once monthly, on Tuesday, on the dates indicated below, a bulk of the dollar value of orders will be placed with the company representatives. On the Friday prior, from 3 P.M. to 5 P.M., the representatives will call the Pharmacy Office by telephone requesting information on items placed on bid. On the Monday prior, from 3 P.M. to 5 P.M., the representatives will call and indicate their company's bid for the respective items. On the Tuesday, the representative will call in person and the order should be ready. This should be of advantage to the company representative.

At the time of the company representative's personal call or "detail", it is anticipated that he will accomplish the following:

1. Detail the latest products released by his company since his last visit.

2. Leave or have the company ship automatically 30 copies of all literature on these newly released products and 30 copies of newly released literature on the older products. This material receives distribution to members of the Pharmacy Committee, to the pharmacist staff and pharmacy residents, and to other areas. The remainder is retained in the Pharmacy Library for use in consultations with the physician, nursing and dental staff members.

3. Advise of the products released for investigational use in the Jefferson Medical College and Hospital, giving the code and other names, the name of investigator, the pharmacologic action, untoward actions, the antidotal or emergency treatment if taken in overdose.

4. Advise of the products released for "clinical trial" in the Jefferson Medical College and Hospital (drugs that have been approved and released by F.D.A.), giving the generic and trade names, the name of the physician who is carrying out the project, the pharmacologic action, untoward actions, and the antidotal or emergency treatment if taken in overdose.

5. Insert *all* price changes in three catalogs of your company which are in the Pharmacy Office, the Inpatient Dispensing Laboratory, and the Outpatient Dispensing Laboratory. At the time of the visit in January, May, and September, please check these catalogs to see that new pages, inserts, etc., are therein and the copies are current.

6. Pick up all return goods.

The restriction of "detailing" once monthly on a specific day is waived for the following reasons:

a. When a new product or device, or special price is released.
b. When the "boss" is in the territory and wants to visit Jefferson.
c. When the representative has a large territory and "passes-thru" Philadelphia infrequently.

On these occasions the representative is requested to make a telephone call for appointment with the Director of Pharmacy Service.

The Director of Pharmacy Service is responsible for all contact with company representatives and is responsible for drug purchases for the Medical Center.

Monthly Detailing Dates 1959

Hours: 9:00 to 11:30 A.M. and 12:15 to 4:15 P.M.

Jan. 6	March 31 (April)	June 30 (July)	Sept. 29 (Oct.)
Feb. 3	May 5	Aug. 4	Nov. 3
Mar. 3	June 2	Sept. 1	Dec. 1

NOTE: On Friday before the above dates, from 3 P.M. to 5 P.M. call Pharmacy (WA-3-1100, Ext. 281) and ask for bid items. On Monday, prior to above, from 3 P.M. to 5 P.M., call Pharmacy and give your quotation.

HERBERT L. FLACK is Director of Pharmacy Service, Jefferson Medical College Hospital, Philadelphia.

A COLD ROOM for the hospital pharmacy

by WILLIAM E. HASSAN, JR. *and* GEORGE STILGOE

► DURING THE CONSTRUCTION OR RENOVATION PLANNING of a hospital pharmacy, much emphasis and consideration is given to such areas as bulk compounding, dispensing, and sterile products manufacturing. However, very little planning is devoted to storage facilities other than to provide the space, shelving, and a biological refrigerator.

A review of the storage requirements of the various drugs in the *Pharmacopeia* and the *National Formulary* indicates that the thermal storage requirements vary from "cold place" to "refrigerator" to "avoid excessive heat or excessive temperature."

WILLIAM E. HASSAN, JR., PhD., is Assistant Director Peter Bent Brigham Hospital and Consultant on Hospital Pharmacy, Massachusetts College of Pharmacy. GEORGE STILGOE is Plant Superintendent, Peter Bent Brigham Hospital, Boston.

Terms Defined

These terms are defined in the fifteenth revision of the *Pharmacopeia* as follows:

Cold place. "A cold place is one having a temperature not exceeding 15°C. (59°F.)"

Refrigerator. "A refrigerator is a cold place in which the temperature is held between 2°C. and 15°C. (36°F. and 59°F.)"

Excessive Heat or *Excessive Temperature.* "Excessive heat or excessive temperature designates temperatures above 49°C. (120°F.)"

Upon comparing these definitions it becomes quite clear that there is no difference in the maximal temperature of a cold place or a refrigerator. On the other hand, it is reasonable to assume that a minimal temperature 2°C. (36°F.) is permissible, thereby making a cold place and a refrigerator identical storage areas in so far as the thermal range is concerned.

Terms Redefined

Because of the above overlapping in the official definitions, we, at the Peter Bent Brigham Hospital, reviewed the thermal storage requirements of the products stored and dispensed by our Pharmacy. The results of our study revealed that three general categories of storage were required: products which must be stored within the range of 2°C. to 10°C. (35.6°F. to 50°F.), those which, according to our professional judgment, would maintain their maximum potency and pharmaceutical elegance at a temperature range of 12°C. to 15°C. (53.6°F. to 59°F.), and those which could be placed in normal shelf storage.

In order to clearly designate the above areas we refer to and define them as follows:

Cold Room. A cold room is an artificially cooled area with a regulated temperature range of 12°C. to 15°C. (53.6°F. to 59°F.)

Refrigerator. A refrigerator is an artificially cooled unit with a regulated temperature range of 2°C. o 10°C. (35.6°F. to 50°F.)

Normal Storage Area. A normal storage area is one in which the maximal temperature does not exceed 49°C. (120°F.) nor the minimal temperature drop below 15°C. (59°F.)

Some of the classes of compounds currently stored in the *cold room* are as follows:

Antibiotics	Ointments and Creams
Biologicals	Oxidized Cellulose
Collodions	Gelatin Sponge Products
Collyria	Suppositories
Fat Emulsions	Syrups

It is quite obvious that in order to store a reasonable inventory of the above products in a refrigerator, many individual units must be made available at a relatively high cost. The simple solution is to use the expensive refrigerator space for those products that must be stored at the lower range of 2°C. to 10°C. (35.6°F. to 50°F.) and to construct a large storage room in which the temperature range can be controlled between 12°C. to 15°C.

Constructing A Cold Room

In building a new pharmacy, the inclusion of a cold room is a relatively simple and not too expensive matter. Piping, wiring, drains, etc. can be installed without incurring the problems which obviously arise in an already built and occupied unit.

In existing facilities, a cold room may be inexpensively constructed if the parties involved will use a little imagination. A little-used corner of the basement storage area should be selected and the necessary area marked-off. If windows are present, they should be bricked-up or at least double-paned and sealed against the outside atmosphere with caulking compound.

An electric light fixture and the required number of electrical outlets should be installed with the switch controlling the light fixture being on the outside wall nearest the entrance to the room.

The necessary additional walls of the room may be constructed of concrete, cinder block, concrete blocks, or brick. Where the use of the above building materials is not feasible, a similar result may be had by the use of wood studs with aluminum foil insulation. The inner side of this type of wall should be cement plastered and the outer side "finished-off" by covering with masonite or other inexpensive material. The door should fit tightly, be no larger than necessary, and be provided with a good automatic door closer.

An electric motor-driven air cooled Freon compressor unit with a remote blower-type cooling coil will provide the necessary refrigeration. This unit should be installed with the necessary thermostat and expansion valve required to maintain the desired temperature range. The blower is mounted in the Cold Room. To it, a small waste line is installed to drain away the condensate which collects on the refrigeration coil. The compressor may be installed outside of the Cold Room in order to conserve space within.

Obviously the size of the Cold Room to be constructed will determine the capacity of the refrigeration unit to be installed. In general, a room approximately 10′ x 10′ x 10′ would require one ton of refrigeration to maintain a temperature range of 50°F. to 60°F.

Once constructed, the room may be equipped with the necessary shelving, storage bins, cabinets, and work bench.

Our experience with cold room storage facilities has spanned four years. During this time we have observed a demonstrable additional life span to many pharmaceuticals currently in use which under normal shelf storage would have deteriorated in a shorter period of time. In addition, the Cold Room has allowed us to purchase in quantity many items on which we normally would have restricted the purchase volume because of the lack of adequate cold storage facilities. Clearly then, a Cold Room should be given a place in the renovation or construction program of a hospital pharmacy.

statement on the

PHARMACY & THERAPEUTICS COMMITTEE

Approved by the Board of Trustees of the American Hospital Association and the Executive Committee of the American Society of Hospital Pharmacists February 1959

Preamble

► HOSPITALS ORGANIZE AND MARSHAL the best professional skills and judgment available to provide care and treatment of patients. The treatment of these patients in many cases is dependent upon the effective use of drugs. The multiplicity of drugs available today makes it mandatory that an organized sound program of activity be developed within the hospital to insure that patients receive the best care and protection possible.

One of the most effective ways of providing this kind of care and protection is by organizing a Pharmacy and Therapeutics Committee. This committee is designed to make maximum use of available professional skills and judgment. The establishment of a Pharmacy and Therapeutics Committee is strongly recommended to all hospitals. It is a measure which supports and enhances the principle of self-government in the area of high drug standards and practices for the medical staff connected with a hospital. Ultimate benefits accrue to the patient in improved patient care and treatment as established voluntarily by the medical staff.

The Pharmacy and Therapeutics Committee

The Pharmacy and Therapeutics Committee is an advisory group of the medical staff and serves as the organizational line of communication or liaison between the medical staff and the pharmacy department. This committee is composed primarily of physicians and the pharmacist and is selected under the guidance of the medical staff. It is also a policy-recommending body to the medical staff and to the administration of the hospital on all matters related to the use of drugs. (This committee does not have intrinsic authority or power of action unless specifically granted such authority.)

PURPOSES

The primary purposes of the Pharmacy and Therapeutics Committee are:

A. Advisory. The committee recommends the adoption or assists in the formulation of broad professional policies regarding evaluation, selection, procurement, distribution, use, safe practices, and other matters pertinent to drugs in hospitals.

B. Educational. The committee recommends or assists in the formulation of programs designed to meet the needs of the professional staff (doctors, nurses and the pharmacist) for complete current knowledge on matters related to drugs and drug practices.

ORGANIZATION

While the composition of the Pharmacy and Therapeutics Committee may vary from hospital to hospital, the following is offered as a guide:

A. The Pharmacy and Therapeutics Committee of the medical staff should be composed of no less than three physicians and the pharmacist, appointed by a governing unit or elected official of the organized medical staff. The hospital administrator or his designated representative should be an ex officio member of the committee.

B. A chairman from the physician representatives should be appointed. The pharmacist is generally designated secretary.

C. The Pharmacy and Therapeutics Committee should meet regularly, no less frequently than twice per year, and should meet on call when necessary.

D. The committee should feel free to invite to its meetings persons within or without the hospital who can contribute from their specialized knowledge or experience.

E. An agenda is desirable and should be prepared and submitted to members of the committee in sufficient time before the meeting.

F. Minutes should be kept by the secretary and should be maintained in the permanent records of the hospital.

G. Recommendations of the Pharmacy and Therapeutics Committee shall be presented to the medical staff or its appropriate committee for adoption or recommendation.

FUNCTIONS AND SCOPE

The basic organization of the hospital and medical staffs will determine the functions and scope of the Pharmacy and Therapeutics Committee. The following list, which is not necessarily comprehensive, is offered as a guide:

A. To serve in an advisory capacity to the medical staff and hospital administration in all matters pertaining to the use of drugs.

B. To serve in an advisory capacity to the medical staff and the pharmacist in the selection or choice of drugs which meet the most effective therapeutic quality standards.

C. To evaluate objectively clinical data regarding new drugs or agents proposed for use in the hospital.

D. To prevent unnecessary duplication of the same basic drug or its combinations.

E. To recommend additions and deletions from

the list of drugs accepted for use in the hospital.

F. To develop a basic drug list or formulary of accepted drugs for use in the hospital and to provide for its constant revision.

G. To make recommendations concerning drugs to be stocked in hospital patient units or services.

H. To establish or plan suitable educational programs for the professional staff on pertinent matters related to drugs and their use.

I. To recommend policies regarding the safe use of drugs in hospitals, including a study of such matters as investigational drugs, hazardous drugs, and others.

J. To study problems involved in proper distribution and labeling of medications for inpatients and outpatients.

K. To study problems related to the administration of medications.

L. To review reported adverse reactions to drugs administered.

M. To evaluate periodically medical records in terms of drug therapy.

Reviewing the Formulary . . . Editorial from Journal of the AHA

► APPEARANCE OF A complete collection of drug monographs in more than 3000 hospital mailboxes during the last month marked the beginning of the American Hospital Formulary Service of theAMERICAN SOCIETY OF HOSPITAL PHARMACISTS. As a part of the service, offered on a subscription basis, subscribers will receive new monographs as new drugs are evaluated.

One of the most important single factors in the service, the ASHP has stated, is that the medical staff of each hospital retains complete authority over drugs to be included in the formulary of the hospital. Thus, working through the Pharmacy and Therapeutics Committee, each medical staff will select from the loose-leaf formulary only those drugs it considers ones of choice. Additional new drugs can be considered by the staff for inclusion in the formulary as monographs are received.

Although the need for some type of formulary service had been recognized and discussed for years, actual work on the American Hospital Formulary Service began in 1954. The service was approved in principle by the Board of Trustees of the American Hospital Association in 1958. It has received similar approval from the Catholic Hospital Association and the American Pharmaceutical Association.

Aside from the obvious advantage of time saved for the Pharmacy and Therapeutics Committee—and the pharmacist as a member of that committee—in preparing drug monographs and compiling a formulary, the medical staff and the committee are given more time for evaluating drugs and attending to other matters related to the distribution and use of pharmaceuticals in hospitals. The service also provides convenient reference for physicians, nurses and pharmacists regarding drugs, their dosage forms, and other pertinent data.

Introduction of the American Hospital Formulary Service focuses attention on the matter of implementing and administering a hospital formulary, whether based on monographs developed in the hospital or by outside sources. Formalities of adopting a formulary, the lines of authority for its administration, the educational aspects of applying it—these and related matters deserve the most careful consideration.

Hospitals adopting the ASHP service can profitably make it an occasion for reviewing their professional policies relating to drugs, making certain that the service is being laid down upon a solid foundation of acceptance and understanding. Hospitals in the latter stages of developing their own formulary can also profit from an appraisal of how well the system will mesh with established policies. The following queries might provide a rough guide for such a review:

- Has the medical staff appointed a Pharmacy and Therapeutics Committee and charged it with the responsibility of formulating broad professional policies regarding the evaluation, selection, procurement, distribution, use, safety procedures and other matters related to drugs in hospitals?
- Are these policies in writing and has the medical staff formally adopted them?
- Do the policies provide for (1) the clinical evaluation of nonformulary drugs by members of the medical staff and (2) the clinical evaluation and control of investigational drugs?
- Has the principle of accepting drugs by their generic names been adopted, even though trade name drugs may be in common use in the hospital?
- Has the medical staff clearly indicated that the formulary system is desirable for the hospital?
- Finally, in the formulation of policies and procedures, has terminology been avoided (such as use of the term "substitution") which impliedly approves the *unauthorized* dispensing of a brand different from that prescribed or the dispensing of an entirely different drug, neither of which takes place under the formulary system?

In addition, many hospitals could profit from a review of their labeling procedures and practices. Attention might be given to problems of correct labeling of pharmaceuticals, with particular reference to the labeling of medications in the pharmacy and on nursing units, being certain that no container carries only a proprietary name when the product is actually made by another manufacturer.

FROM: *Hospitals* (Editorial) *33*:25 (Feb. 1) 1959.

suggested principles of

RELATIONSHIP BETWEEN SMALLER HOSPITALS AND PART-TIME PHARMACISTS

who provide pharmaceutical services

Approved by the Board of Trustees of the American Hospital Association and the Executive Committee of the American Society of Hospital Pharmacists February 1959

Preamble

► ALL HOSPITALS should be cognizant of the contribution made by a sound and organized pharmaceutical service for improved patient care and treatment. The introduction annually of numerous potent drugs requires that all hospitals have the full or part-time service of a registered pharmacist. In small hospitals which cannot obtain or afford a full-time hospital pharmacist, the services of a pharmacist on a part-time or consultative basis may be obtained.

If the services of a hospital pharmacist of another hospital are not obtainable, the services of a local registered pharmacist should be utilized whenever possible. When pharmaceutical service from a local pharmacy is considered, the part-time pharmacist and the hospital might consider certain guiding principles of affiliation. The Principles of Relationship Between Smaller Hospitals and Part-time Pharmacists are suggested to achieve the objective of better patient care.

Basic Principle

1. *The pharmaceutical service of the hospital shall be organized and maintained primarily for the benefit of hospital patients.*

In any hospital, the individual elements which are maintained and coordinated are all subordinate to the main objective of providing care to the sick and injured. Any function either newly added or strengthened, as in this instance drug or pharmaceutical services (from any source whatever or by any arrangement), must be in agreement with this basic principle.

Organization

1. *The hospital pharmaceutical service should be under the direction of a professionally competent, legally qualified pharmacist.*

The hospital must exercise due care in its selection of personnel. The hospital safeguards the patient and its public trust by fixing the responsibility for its varied functions by appointing adequately qualified individuals.

2. *A part-time pharmacist, as a professional member of the hospital staff and as the head of a hospital function or department, must assume the responsibilities involved.*

Recognition as a member of the hospital organization will be in direct proportion to the responsibility which the individual is capable of accepting on a part-time basis.

3. *The part-time pharmacist shall be responsible to the proper administrative authority of the hospital for developing, supervising and coordinating the activities of the pharmaceutical services to hospital patients and departments.*

With hospital affiliation, an attendant responsibility is placed on the part-time pharmacist to preserve the unity and coordination of the hospital's component activities as directed by the administrator in policies laid down in behalf of the public which the hospital governing board represents. Thus the part-time pharmacist subscribing to a hospital connection in terms of relationships, is primarily responsible to the hospital administrator for those services provided to hospital patients and departments.

Rules, regulations and procedures regarding drug services to hospital patients and departments should not be counter to or in opposition to the hospital's policies for patients as interpreted and approved by the hospital administrator in behalf of the medical staff, and of the hospital governing board and the public it represents.

4. *The organization of hospital pharmaceutical services, the relationship to the hospital and its elements, and the specific services to be provided should be outlined and reviewed periodically by the hospital administrator and the part-time pharmacist who provides pharmaceutical services to hospital patients and departments.*

To keep abreast of changing developments or staff demands for high standards of service and to obviate misunderstandings, relationships should be outlined initially and reviewed periodically. This appears to be particularly necessary in those situations where certain elements of services are provided on the hospital premises, and others in varying degrees emanate from sources away from the hospital environment arranged by delegation to others who may be unfamiliar with hospital safeguards and policies.

5. *The organization of pharmaceutical services should include the utilization of an organized Pharmacy and Therapeutics Committee responsible for the development of rules and regulations pertaining to professional policies related to pharmaceutical services for hospital patients.*

Following the usual practice in hospitals, the medical and pharmacy staffs acting in an advisory capacity are the most qualified to recommend to the hospital such policies as relate to selection, evaluation and distribution of drugs used in the hospital. The composition and specific objectives of the Pharmacy and Therapeutics Committee as well as its appointment may be developed to best meet the needs of the hospital and its standards.

Functions

1. *The primary functions of the service provided by a part-time pharmacist should be to furnish drugs with sufficient dispatch so that patient care will not be hindered, to provide adequate safeguards for the patient and hospital personnel, and to provide therapeutic agents of respected quality.*

Responsibilities do not begin or end with filling prescriptions or furnishing drugs remotely from the hospital. The well-rounded and minimum responsibility might include such personal services by the part-time pharmacist as staff education related to safeguards in use of drugs on the premises, contribution to educational or research programs where extant, provision of maximum consultation services to nursing and medical staffs, inspection of drug storage and distribution throughout the hospital, attendance at committee and department meetings, preparation of fiscal and professional reports where necessary, maintenance of an approved stock of emergency drugs, provision for 24-hour drug services, elimination of waste, etc.

2. *Records concerned with hospital patient services should be maintained separately, preserved for the period prescribed by legal or hospital requirements, and be readily available.*

Such records as narcotic, barbiturate, alcohol, prescription, and requisition requests differ between hospitals and retail pharmacy practice. Identification with a hospital transaction or treatment may be of prime importance.

3. *The relationship between the hospital and the part-time pharmacist in the function of drug procurement or purchasing for both patient and general hospital use should be based on fixed responsibilities and meet the following principles on Business Relationships.*

The smaller hospital generally purchases supplies through a modified central channel in the organization. The need for expert evaluation of specifications in the drug field is recognized. Hospitals contributing services to indigent patients enjoy special price privileges, and drugs in this category ethically should not be diverted to other outlets. The complexity in the area of procurement and possibility of abuses by either the hospital or the part-time pharmacist require careful evaluation of the procedure.

a. That basis of financial arrangement between a hospital and part-time local pharmacist should be followed which would best meet the local situation. It is recognized that no one basis would seem applicable or suitable in all instances.

The hospital and the part-time pharmacist must have a thorough appreciation of each other's business systems and controls. This may involve detailed exploration.

b. Arrangements involving services to patients through voluntary insurance, indigent patients, or employees should be established in accordance with accepted hospital relationships and philosophies involving such programs.

Some insurance plans vary between localities, and in some instances the so-called "no-pay or part-pay" patients comprise a sizable number of persons. Special financial arrangements in accord with hospital policy for other services provided may be required.

c. Arrangements for a regular schedule for the personal services of the part-time pharmacist on the hospital premises should be made on a flexible basis related to time spent and services provided.

The hospital schedule and its 24-hour service to patients demands a varying amount or period spent during regular visits or to meet emergency requirements. In general, an average amount of time may be considered initially. Such an arrangement should be included in a plan, even though many services are provided remotely from the hospital premises.

d. Solicitation of patients or rendering services to the medical staff for their private practice through hospital channels by any person connected with the hospital is unethical.

The privilege of hospital affiliation should not be used to gain unfair advantage over other members of the profession. Patients and physicians are attracted to a particular pharmacy because of its known merit and established reputation for satisfactory service. Implied or open solicitation through hospital connections should not be indulged in by part-time pharmacists.

e. Relationships between a part-time pharmacist and the hospital are considered on the

merit of reputable, prompt service to patients at reasonable cost, ability to serve the hospital in all phases of pharmacy service demanded by hospital requirements, and should subscribe to the suggested principles.

In communities where several pharmacies are available, a hospital may hesitate to engage the services of any one pharmacist because of pressures and ill-feeling against the hospital by other pharmacists. Intra-professional rivalry should not place the hospital in a position of not raising its own pharmacy service standards. The hospital as a community institution should be allowed the privilege of judging its future relationships for expanded services on the basis of a part-time pharmacist's ability to provide those services in the spirit in which patient care is provided in that hospital.

Conclusion

These Principles of Relationship Between Smaller Hospitals and Part-time Pharmacists for Hospitals are suggested. These recommended guides for further development and discussion are a beginning for those hospitals and pharmacists who wish to explore possibilities for developing higher standards of pharmaceutical service in institutions without full-time pharmacists.

A combination of such principles and the Minimum Standard for Pharmacies in Hospitals can provide both smaller hospitals and part-time pharmacists a working basis for a higher level of pharmaceutical service.

THE AMERICAN HOSPITAL FORMULARY SERVICE

► THERE HAS BEEN CONSIDERABLE DISCUSSION on the Hospital Formulary Service which is to be supplied by the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, and it is important to recognize of what this service consists.

There has been great demand from individual hospitals for information on drugs which the average hospital pharmacy must stock in order to meet the requirements of its individual staff.

It was considered most efficient to prepare one set of monographs giving all essential information regarding drugs, which would be considered thoroughly authentic, and make these monographs available to all hospitals. The individual hospital would thus be in a position to develop its own Formulary or "Drug List" on the basis of selections made by the Therapeutics Committee of its Hospital Staff.

The AMERICAN SOCIETY OF HOSPITAL PHARMACISTS set up the necessary committee and staff to prepare a comprehensive list of monographs covering practically all important drugs which might be used in the treatment of hospital patients.

These monographs have been compiled with an eye to giving as complete information as possible, including official titles, trade names, and synonyms. The Therapeutics Committee and the hospital pharmacist who generally acts as secretary of this committee, need not, therefore, concern themselves with the authenticity and scope of information made available. Their function in preparing their own Hospital Formulary based on the American Hospital Formulary Service, becomes one of selection of the monographs to be included. By a loose-leaf arrangement, both the American Hospital Formulary Service and the individual hospital formularies can be revised, enlarged, or reduced as drugs for which monographs become available are added to the armamentarium of the prescriber or as they fade into obsolescence.

In the development of standards for pharmacy in hospitals it has been made clear by the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS that there is no effort on its part to cast all pharmacies into the same mold. It is well recognized that each hospital must adjust the extent of its services to the requirements of its clientele.

The medication which a patient receives, be it in private practice, in group practice or in hospitals, depends upon the prescriber. He is the judge of what his patient should receive in the way of drugs. No change may be made ethically or lawfully in dispensing prescriptions, without the consent of the prescriber. This applies throughout the practice of medicine and pharmacy. If the prescriber desires a certain brand of a drug, that is his prerogative and it is the business of the pharmacist to supply that brand. If the prescriber wishes to change the brand of the drug for good and sufficient reasons, that is also his prerogative. Pharmacists would be well advised to keep authentic records of any changes requested or agreed to by the prescriber, if the original prescription is changed in any manner.

We believe that the American Hospital Formulary Service will prove very useful to hospitals, and we have the utmost confidence in those who will make the service available, as well as in those who will make use of the service, that the legal, technical, professional, and proprietary rights of all concerned will be observed.

FROM: Straight From Headquarters by Robert P. Fischelis, *J. Am. Pharm. Assoc., Pract. Pharm. Ed.* 20:23 (Jan.) 1959.

Therapeutic Trends

edited by WILLIAM JOHNSON

U-8614

U-8614, a synthetic C_{12}-desoxysteroid, was given by mouth to 5 patients with normal adrenal function 15 to 20 mg. a day in fractional doses which suppressed adrenocortical secretion. In all but one patient plasma and urinary corticoids approached zero during the four to six day period of administration of U-8614. Suppression of urinary corticoids was apparent on the first day of the test period. When administration of U-8614 was stopped, the urinary corticoids returned to normal within a 24-hour period in four patients, and after four days in the fifth patient. A woman with Cushings syndrome due to adrenal hyperplasma, received U-8614 in a dosage of 20 mg. a day for six days. This resulted in some suppression of both urinary corticoids and 17-ketosteroids. It is strongly suggested that U-8614 inhibited the production or release of corticotropin (ACTH). In order to determine whether U-8614 was affecting adrenal function at the level of the adrenal gland, an intravenous ACTH test was performed on a patient receiving U-8614. The response of the plasma corticoid level to the ACTH was normal and of the same magnitude as in a subsequent test performed on the same patient during a control period. In order to explore other indices of corticoid activity, U-8614 was given to 2 hypophysectomized patients who were in a state of adrenal insufficiency following withdrawal of maintenance cortisone. U-8614, in a dosage of 15 mg. a day, led to restoration of the eucorticoid state within 24 hours. So far it is concluded that U-8614 possesses many of the activities of hydrocorticone and is somewhat more potent than hydrocortisone. The activity of this compound, lacking what was previously assumed to be an essential functional group, may point the way towards even more selective modifications of the steroids. This study was reported by Lipsett and Bergenstal in *J. Clin. Endocrinol. Metabolism 18*:790-792 (July) 1958. U-8614 was supplied by the Upjohn Company.

W. E. HERSHBERGER

Demethylchlortetracycline—A New Antibiotic

The new antibiotic demethylchlortetracycline (DMCT) is found to be much more active than tetracycline against *B. cereus* No. 5, Str. 98, and *Staph.* 209P organisms. DMCT produced significantly higher and better sustained levels of activity than tetracycline against these organisms after similar oral doses by weight. The comparisons of the levels after single doses of 500 mg. in the initial study were only preliminary and were not strictly controlled, but suggested that DMCT may be absorbed slightly less rapidly than tetracycline. DMCT, however, has a greater "half life" in serum which was about 44 percent longer than that of tetracycline. "Half life" is the time required for the level of a drug to drop to half that determined at any given time. The levels of activity against all three test organisms were higher after each successive dose of DMCT, and the differences were all greater 12 hours after each corresponding dose than they were in four hours. This longer "half life" is probably wholly or largely dependent on the slower rate of renal clearance of DMCT which was only about 43 percent as fast as that of tetracycline. The superiority of the activity of DMCT is all the more impressive because the study on repeated doses was carried out under normal dietary conditions and was otherwise carefully controlled for comparability of conditions. These findings indicate that smaller and less frequent doses of DMCT as compared with tetracycline may be required to produce the same systemic antibacterial effects *in vivo*. Further study will be required to learn the relative activity of DMCT against a variety of species and strains of susceptible micro-organisms and the relative toxicity of this antibiotic when it is given under clinical conditions. This work was reported by Kunin and Finland in *New Eng. J. Med. 259*:999 (November) 1958. Tetracycline and DMCT were supplied as Achromycin V and Achromycin AVIII by Lederle Laboratories.

SYLVIA SCHMIDT

Glycyrrhetic Acid—Anti-Inflammatory Drug

A study of the pharmacological properties of glycyrrhetic acid, a new anti-inflammatory drug from licorice, shows that it has an extremely low toxicity and is non-irritant to the skin. It has been confirmed that exceptionally large doses of glycyrrhetic acid in animals give an antidiuretic action associated with changes in the metabolism of sodium and potassium, but do not cause kidney damage. Water retention was not seen, however, with small doses used in human volunteers. The low solubility of glycyrrhetic

acid in body fluids has so far precluded parenteral administration in man, but this will be made possible with development of more soluble derivatives which may prove of value in rheumatic diseases. Finney *et al* in *J. Pharm. Pharmacol. 10*:687 (November) 1958 relate that an important property of glycyrrhetic acid is its complete freedom from glucocorticoid-like actions, a serious disadvantage with the corticosteroids. While it has been shown that little absorption of these steroids occurs through normal skin, this cannot be assumed in dermatological conditions where the protective dermal layers may be broken. Much remains to be discovered about the mode of action of glycyrrhetic acid, but the drug offers a new approach to the treatment of inflammatory conditions free from the disadvantages of corticoids which have claimed so much attention. This disproves the concept that an anti-inflammatory agent must of necessity have a concomitant corticoid-like action. Glycyrrhetic acid was supplied by Biorex Lab. Ltd. London.

SYLVIA SCHMIDT

IsoBilagol—Treatment Of Biliary Tract Disease

A group of 38 patients with biliary tract disease were treated with a preparation containing d-glucitol and diisopromine (IsoBilagol). The diisopromine was used to reinforce the relaxant action of d-glucitol on the sphincter and to overcome biliary tract spasm. Of those patients treated, N. Chaikin reports in *Am. J. Gastroenterology 30*:505 (November) 1958 that none became worse, 13.1 percent showed no improvement, 47.3 percent moderate improvement, and 39.4 percent marked improvement. Significant statistical improvement occurred in those cases with chronic cholecystitis with no evidence of stones, delayed emptying of the gall bladder, and post cholecystectomy syndrome. Significant improvement was also noted in the areas of fat tolerance, nausea, abdominal discomfort, eructations, and constipation; improvement of a lesser degree occurred in the cases with pain. Except for one patient whose nausea increased, none of the patients showed any toxic effects. IsoBilagol is a good well-tolerated cholecystokinetic for the treatment of biliary tract disease and merits further study. This drug was supplied by Purdue Frederick Co., New York, N. Y.

SYLVIA SCHMIDT

PM-671—A New Drug For Petit Mal Epilepsy

Zimmerman and Burgemiester reported in *Neurology 8*:769 (October) 1958 on the usage of PM-671. The drug, a succinimide compound, offers more promise than any other succinimide compound tested in the last six years. Its primary effect is against petit mal attacks. The side effects are mild, and it has a notable holding power. Quick and dramatic reduction of attacks occurred in most of the 109 patients treated in this study. Two side effects encountered were drowsiness and dizziness. Evidence that PM-671 is essentially a petit mal drug appeared when cases of pure petit mal and mixed petit mal were tested. The cases of pure petit mal responded more favorably than the mixed conditions. In the patients treated in the study, complete control was obtained in 42 percent, practical control in 24 percent, and partial control in 26 percent.

RICHARD H. HARRISON

Furazolidone—Antihypertensive

Furazolidone, a known antimicrobial agent, was found to have some effect on the hypertensive state. A study was made by Calesnick to determine the effectiveness and mode of action. The results were related in the *Am. J. Med. Sci. 236*:736 (Dec.) 1958. Sixteen patients, the majority of them ambulatory, were selected for treatment. No attempt was made to restrict either salt or caloric intake. The patients were observed at weekly intervals. Dosages were started at 800 mg. daily (200 mg. four times daily) and gradually reduced. The main side effect was nausea, which seemed to diminish or disappear with continued treatment. Normotensive blood pressure was unaltered and, once a stable plateau of the pressure was reached, increased dosage did not lower the pressure further. This experiment demonstrates that furazolidone will produce a gradual reduction of arterial blood pressure in patients with primary hypertension. The drug is still under investigation to determine the mode of action.

RICHARD H. HARRISON

Trimeglamide—Sedative and Soporific

In an investigation of new central nervous system compounds trimeglamide, trimethoxybenzoyl-glycine-diethylamide (Riker 548), demonstrated the ability to induce in animals a state of somnolence which could not be distinguished from the physiologic state of sleep. This somnifacient action was neither preceded nor followed by accompanying ataxia in dogs and cats. A five- to ten-fold increase of the soporific dose resulted in restlessness and disorientation instead of sleep. In man, oral doses of 500 to 1500 mg. of trimeglamide caused sedation or drowsiness, or both, in half the cases. No spindling or drug-induced artifacts were found in electroencephalographic recordings. This new advantageous sleep-inducing drug was furnished by Riker Research Division and reported by Cronheim *et al* in *Science 128:*1570 (Dec. 19) 1958.

SYLVIA SCHMIDT

Timely Drugs

Deronil

GENERIC NAME: Dexamethasone.
INDICATIONS: Same as those for prednisone or prednisolone, and comprise various rheumatic, allergic, dermatologic, ocular and other conditions known to be responsive to corticosteriod therapy.
SIDE EFFECTS AND CONTRAINDICATIONS: Any of the reported side effects of other such compounds; as with other steroids, recurrence or complications of peptic ulcer may occur during therapy; contraindicated in herpes simplex of the eye.
DOSAGE: Individually determined.
PREPARATIONS: Tablets of 0.75 mg.
PACKAGING: Bottles of 50 and 500 tablets.
SUPPLIER: Schering Corp.

Diupres

COMPOSITION: Chlorothiazide (Diuril) and reserpine.
INDICATIONS: Greater antihypertensive effect than either ingredient alone; fewer and less severe side effects; lessens need for dietary salt restriction; indicated for every degree of hypertension.
SIDE EFFECTS AND CONTRAINDICATIONS: Has usual side effects and precautions of individual components.
DOSAGE: Range of 1 tablet daily to 1 tablet 4 times daily.
PREPARATIONS: Diupres-250 contains chlorothiazide 250 mg. and reserpine 0.125 mg.; Diupres-500 contains chlorothiazide 500 mg. and reserpine 0.125 mg.
PACKAGING: Bottles of 100 and 1,000 tablets.
SUPPLIER: Merck Sharp & Dohme.

Furacin Cream

GENERIC NAME: Nitrofurazone.
INDICATIONS: Vaginal cream to control infection and speed healing after delivery, surgery, radiation and office gynecological procedures.
SIDE EFFECTS AND CONTRAINDICATIONS: Frequency of sensitization is less than 1 percent, but may occur in allergic patients or those with abnormally sensitive skins.
PREPARATIONS: Cream containing 0.2% nitrofurazone.
PACKAGING: Tubes of 3 ounces, with plastic, plunger-type vaginal applicator.
SUPPLIER: Eaton Laboratories.

Medaprin

COMPOSITION: Methylprednisolone (Medrol), acetylsalicylic acid, and calcium carbonate.
INDICATIONS: Mild to moderate acute rheumatic and musculoskeletal conditions; also for maintenance therapy in nonsevere and chronic conditions.
SIDE EFFECTS AND CONTRAINDICATIONS: Tuberculosis, renal insufficiency, peptic ulcer, acute psychosis, Cushing's syndrome, herpes simplex keratitis; should be used with caution in presence of infection, diabetes, osteoporosis, chronic psychotic reactions, hypertension, and congestive heart failure.
DOSAGE: One or 2 tablets three or four times daily, after meals and at bedtime
PREPARATIONS: Tablets containing methylprednisolone 1 mg., acetylsalicylic acid 300 mg., and calcium carbonate 200 mg.
PACKAGING: Bottles of 100 tablets.
SUPPLIER: Upjohn Co.

Prozine

COMPOSITION: Meprobamate (Equanil) and promazine (Sparine) hydrochloride.
INDICATIONS: In patients with a primary emotional disturbance, emotional disturbance unrelated to their organic disease, and emotionally disturbed by primary organic disease; controls moderate to severe emotional disturbance.
SIDE EFFECTS AND CONTRAINDICATIONS: Drowsiness may occur in first 24 hours; rarely, allergic reactions; contraindicated in comatose states caused by alcohol, barbiturates, opiates, or in patients in whom a drop in blood pressure may be undesirable.
DOSAGE: One or 2 capsules three or four times daily.
PREPARATIONS: Capsules containing meprobamate 200 mg. and promazine hydrochloride 25 mg.
PACKAGING: Bottles of 50 capsules.
SUPPIER: Wyeth.

Simron

COMPOSITION: Ferrous gluconate and polyoxyethylene glucitan monolaurate (Sacagen).
INDICATIONS: Iron hematinic with special absorption agent; better absorption, freedom from side effects.
DOSAGE: One capsule three times daily, which supplies 30 mg. elemental iron as ferrous gluconate.
PREPARATIONS: Capsules containing ferrous gluconate 10 mg. and polyoxyethylene glucitan monolaurate 400 mg.
PACKAGING: Bottles of 100 capsules.
SUPPLIER: Wm. S. Merrell Co.

Stenisone

COMPOSITION: Prednisone, methandriol, magnesium trisilicate, dried aluminum hydroxide gel, calcium carbonate, magnesium carbonate, Regonol (vegetable gum), and Egraine (oat binder).
INDICATIONS: Provides increased safety in adrenal corticosteroid therapy; contains methandriol, a relatively non-virilizing anabolic steroid, which helps to counteract the catabolic osteoporotic effects of prednisone; and contains antacid ingredients.
DOSAGE: Individually determined.
PREPARATIONS: Tablets containing prednisone 5 mg., methandriol (methylandrostenediol) 20 mg., magnesium trisilicate 100 mg., dried aluminum hydroxide gel 60 mg., calcium carbonate 70 mg., magnesium carbonate 40 mg., Regonol 66.6 mg., and Egraine 30 mg.
PACKAGING: Bottles of 30 and 100 tablets.
SUPPLIER: Organon, Inc.

Notes + Suggestions

edited by CLIFTON J. LATIOLAIS

LIQUID FILLING MACHINE

The Liliput* is a semi-automatic liquid filling apparatus particularly adapted for filling narrow mouth bottles, vials and ampuls ranging from 0.5 ml. to 250 ml. capacity.

The filling output per hour ranges up to 3000 units depending on the diameter of bottle opening and the liquid to be dispensed. Viscous liquids may be prepackaged with the Liliput. Standard stroke settings supplied with the unit allow for proportioning 5, 10, 20, 30, 50, 100, 150 and 250 ml. quantities of liquid per stroke.

The Liliput Filler is approximately 65 x 45 x 35 cm., weighs 45 Kg. and costs $622.70. (2600 German Marks)

*Available from Rudolph W. Fritsch, Richard-Wagner- Str. 42, Bayreuth, Germany.

AEROSOL CAN DISPOSAL

The disposal of aerosol containers in incinerators may lead to accidents due to incinerator explosions. These may be eliminated by simply piercing a hole in the pressurized container. A piercing head unit is available for this purpose from Builder's Products, 108-110 Wooster St., New York 12, New York for $15.00. This piercing head unit fits all size aerosol cans.

NECTADON SYRUP 10 MG. PER 5 ML.

The following formula for Nectadon* Syrup is suggested in Merck's recently released brochure A-170 entitled "Nectadon—Suggested Pharmaceutical Formulations."

Nectadon	0.2	Gm.
Tartaric Acid, N.F.	0.2	Gm.
Sucaryl Sodium	0.2	Gm.
Potassium Guaiacolsulfonate, N.F.	1.7	Gm.
Chloroform	0.08	Gm.
Sodium Benzoate, U.S.P.	0.10	Gm.
Mint Green (Hercules)	0.004	Gm.
Flavor 4061 (Ungerer)	0.13	ml.
Cherry 59.088T (Firmenich)	0.03	ml.
Peppermint Oil 10% in Alcohol	1.0	ml.
Distilled Water	10.0	ml.
Sorbitol Solution N.F., to make	100.0	ml.

Dissolve the tartaric acid in the water (heated to 50° C.). Dissolve the Nectadon in the tartaric acid solution. Add about half of the sorbitol solution. Dissolve the Sucaryl, sodium benzoate and potassium guaiacolsulfonate in the above solution.

Mix the chloroform with the alcoholic peppermint solution and add to the first solution and mix. Then add the dye (dissolved in a small amount of water) and the flavors and mix well. Filter and make up to volume with the sorbitol solution.

*Nectadon is Merck's trade name for noscapine (formerly called narcotine).

SILICONE HAND LOTION

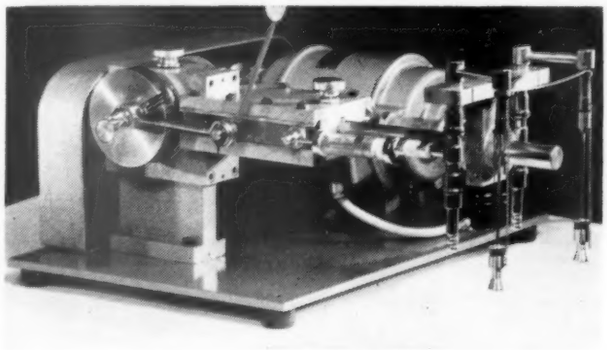
Silicone, DC 200 Fluid 100 Cstks.	5.0%
Light Liquid Petrolatum	10.0%
Arlacel 169 (Atlas Powder Co.)	3.0%
Hystrene S-47 (The Humko Co.)	1.0%
Beeswax USP (Bleached)	0.5%
Sodium Borate	0.5%
Distilled Water	80.0%
Preservative, Perfume, Color	q.s.

Mix all the ingredients (except the perfume). Heat to 165-170° F. with high speed agitation. Cool slowly with agitation to about 120° F. and add perfume. Then cool rapidly to room temperature and package.

*From Dow Corning brochure "Silicones in Cosmetics" dated March 1958.

LABORATORY HOMOGENIZER

The Aero-Seal Chemixer* is a laboratory model homogenizer for small scale blending, emulsifying, and homogenizing procedures. Production capacity varies from 100 ml. to over 4000 ml. by simply using ap-

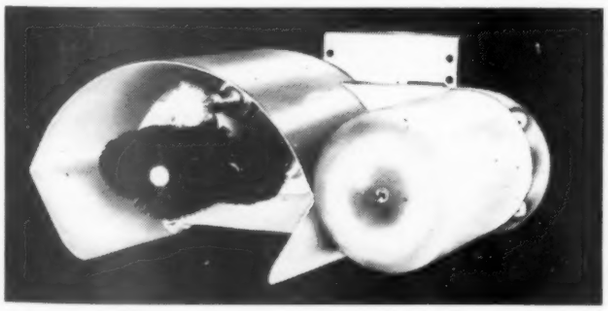


propriate containers. Advantage of the Chemixer is that the aerosol-free assembly eliminates harmful aerosols (whipped-in air) often encountered in homogenizing or blending operations. The stainless steel blades or impellers operate at speeds from 100 to 17,000 RPM using a 1/5 H P motor. Cost of this unit complete with a 5 liter flask is $237.00. Different size Pyrex containers are available at extra cost.

*Harshaw Scientific Division, Harshaw Chemical Co. 1945 E. 97th. St. Cleveland 6, Ohio.

GLASSWARE WASHER

Model C W All Purpose Laboratory Glassware Washer* is a versatile unit for washing varied sizes and shapes of glassware. This washer is equipped with three sets of bottle guides with their proper brushes. Each guide automatically centers the brush with the piece of glassware to be washed so the brush goes right in. This eliminates waste motion and

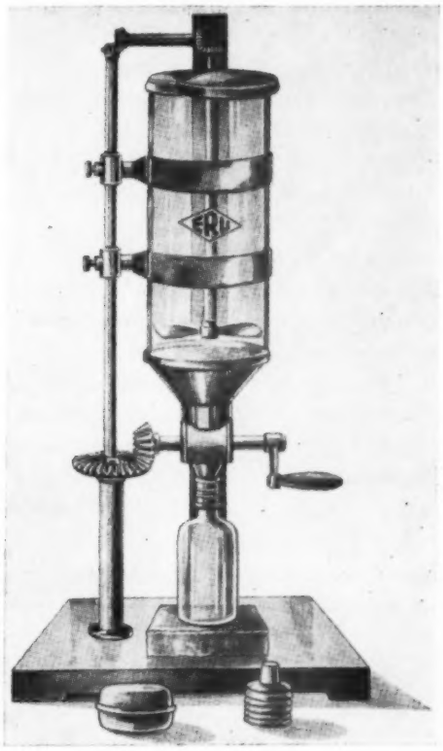


permits "production line" speed. The bottle brush will penetrate to a 10½ inch depth and the spindle diameter permits washing through a minimum 7/16" diameter bottle neck opening. As a bottle washer, the capacity is estimated at between 1000 to 1100 bottles per hour. These washers are portable; no plumbing connections required. Approximate price $159.50 F.O.B. Rockville, Maryland.

*The Lofstrand Co., Rockville, Maryland.

POWDER FILLING APPARATUS

The Novelty Powder Filling Apparatus* is a practical unit for filling or prepackaging pharmaceutical powders in the hospital pharmacy. This filling unit has an attached stirrer which causes the powder to sift down through the filling socket and into the container simply by turning a handle. By a simple vertical adjustment the powder filler may be raised



or lowered to accommodate different size bottles. Interchangeable filling sockets are available for bottles of different sized openings. Electromagnetic vibration tables are available on which the containers are placed to facilitate more accurate filling of powders which tend to clump. The current price of this unit delivered in the United States is $227.00 for the 2, 5, or 10 liter container size.

*Available from Rudolph W. Fritsch, Rich.- Wagner- Str 42, Bayreuth, Germany.

PYRILAMINE MALEATE FORMULATIONS

"The Pharmaceutical Aspects of Pyrilamine Maleate" is the title of Merck's recently released Technical Service Bulletin No. P.M.-2.* This bulletin contains suggested pharmaceutical formulations of pyrilamine maleate tablets, ointments, syrups, creams and nasal solutions. In addition, the chemical and physical properties, compatibilities, labeling information applications and toxicology of pyrilamine are described.

*Available at no charge from Merck and Co. Inc. Rahway, N.J.

News

Ohio State Announces Graduate Program In Hospital Pharmacy

The College of Pharmacy and The Health Center of The Ohio State University announce the beginning of a combined Graduate Study-Internship Program in Hospital Pharmacy on September 1, 1959. Upon satisfactory completion of the program the Master of Science degree will be conferred by The Ohio State University and a Certificate of Internship in Hospital Pharmacy will be awarded by The University Hospital.

Appointments are for a period of twenty-two months, beginning September 1, 1959. During the academic years the intern will devote half-time to the internship program and half-time to graduate study. Full time training in The University Hospital Pharmacy will be required during the summer of 1960.

A stipend of $1800 per year is provided the intern by The University Hospital. The appointment also carries a waiver of non-resident fees and laboratory fees.

Applicants must be graduates of an accredited College of Pharmacy and must meet the requirements for admission to the Graduate School.

Letters of application and requests for further information should be forwarded to Dean Lloyd M. Parks, College of Pharmacy, The Ohio State University, Columbus 10, Ohio.

Philadelphia College Offers Parenteral Products Course

For the sixth consecutive summer a post graduate course in the preparation of parenteral products will be available at the Philadelphia College of Pharmacy and Science.

Starting July 13 and continuing through July 24, the two-week period will include lectures, laboratory exercises, and field trips. The lectures wil cover a variety of topics in the parenteral products field, and in the laboratory a series of small volume parenteral products will be prepared through the cooperative efforts of all who are participating. Opportunity will be provided, also, for field trips to nearby hospitals and manufacturing establishments.

Dr. Kenneth E. Avis, Associate Professor in Pharmacy, has provided a course at the Philadelphia College in this specialized area of Pharmacy for several years at both the graduate and undergraduate levels. He has also conducted the five previous summer courses and will again be in charge of the 1959 program. The course will be open to all persons with training and experience adequate for a basis upon which to build the specialized pharmaceutical techniques required for the preparation of parenteral products, and it has been designed to provide a foundation for those persons who desire to assume or increase their responsibilities in the area of this pharmaceutical specialty; and for more experienced persons, who desire the stimulation of re-thinking fundamental concepts.

The fee for the complete two-week course is $100.00. Early registration is urged through the Registrar of the Philadelphia College of Pharmacy and Science, 43rd Street, Kingsessing and Woodland Avenues, Philadelphia 4, Pa.

International Pharmaceutical Students' Federation Announces Congress

The International Pharmaceutical Students' Federation has issued an invitation to all pharmacy students and recent graduates to attend its VI Congress, which will be held at Noordwijk on Sea, The Netherlands, from September 5-16, 1959. Accommodations at this beautiful Dutch North Sea resort will be in rooms with two to six beds, and a large lounge will be at the disposal of the participants. The program includes general meetings, excursions, social evenings, council meetings, films and a farewell dinner. The all-inclusive charge for the full 10 days is only $38.50.

All young pharmacists and students who will be in Europe this summer are urged to include this Congress in their plans. Those who have attended previous I.P.S.F. meetings have unfailingly called them wonderful experiences they will cherish for years. One leaves having made lasting friendships with future pharmacists from all over the world.

The detailed program will be available shortly. Those interested should send a letter of application, preferably by April 30, to:

Mario van Geijn, Secretary
Rapenburg 47
Leiden, The Netherlands

At the time of application, it is necessary to send a deposit of $7.00 to: Amsterdamsche Bank, Leiden, Netherlands. Please make checks or money orders payable to: Conto Jonkers c/s Congress.

Pharmacist Exchange Program

An invitation to young American pharmacists and pharmacy students to participate in the 1959 Student Exchange Program was issued this week by the International Pharmaceutical Students' Federation. The program offers an opportunity to obtain experience in the way of life and the pharmacy of other lands.

Through its Committee on Student Exchange the Federation will help arrange for young Americans to go to a foreign land to work or observe in a phar-

macy. Pharmacists who have graduated within the past seven years, as well as pharmacy students, are eligible for the program. There are likewise pharmacy students or recent graduates overseas who are eager to know America better, and pharmacists who would be interested in being host to one of the young colleagues for one to several months are being sought. The host pharmacist would be expected to pay a salary at least covering living expenses of the visitor-employee of his choice. The young person going overseas provides his own passage fares. Exact arrangements are worked out by the two parties concerned once contact is established, the Federation points out.

The exchange program has been developed with the idea that it will not only offer a stimulus to the profession and participating individuals, but in its own way will encourage better international understanding.

Pharmacists or students interested in the program may obtain further information from:

Dr. Jerome A. Reinstein, U.S. Liaison Sec'y, IPSF
Chas. Pfizer & Co., Inc.
11 Bartlett Street, Brooklyn 6, New York

The deadline for applications for exchanges this summer is May 15, 1959.

The following categories of participants in the program have been set up:

I. *Exchange Categories*

A. *Those Wishing to Work* in retail or hospital pharmacy for a period of one to three months. Usually the period is one month. (Working students must have completed a year's practical experience.)

B. *Those Wishing to Observe* the work in a pharmacy and the pharmacy students' way of life in another country.

II. *Reception Categories*

A. *Pharmaceutical Families—i.e.,* a family where a parent is a pharmacist and a son or daughter is a pharmacy student. If the latter so desires a direct exchange with the student being visited will be arranged (before or after the visit).

B. *Pharmacists*—without sons and daughters in pharmacy who, nevertheless, would be willing to allow a foreign pharmacy student to work in their retail or hospital pharmacy or manufacturing establishment.

C. *Pharmacy Students*—who are in a position to entertain foreign students. Again, if the host student so desired, every effort would be made to effect a direct exchange.

Southeastern Society to Meet in Atlanta

The Southeastern Society of Hospital Pharmacists will hold its annual meeting April 8-10, 1959, in Atlanta. The meeting will be concurrent with the annual meeting of the Southeastern Hospital Conference. Hospital pharmacists in the Southeast are being urged by Program Chairman Terry B. Nichols of Atlanta to make reservations at the Peachtree Manor which is headquarters for the pharmacists' group.

The program for the three-day meeting will include clinical, legal and administrative papers presented by professors from Emory University School of Medicine, pharmacy professors from the University of Georgia and the Southern College of Pharmacy, and by a representative from the U. S. Public Health Service in Washington, D. C.

Those who will appear on the program are: Dr. Carl Pfeiffer, Emory University, with the subject "Acetylcholine and Behavior;" Dr. Harrison Reeves, Emory University, whose subject will be "Clinical Agents Used in Treatment of Cancer;" two papers will be presented by Dr. George Archambault, U.S.P.H.S., including "The Law of Hospital Pharmacy" and "The Pharmacy of Tomorrow in the United States;" Dr. Frank Groner of Memphis, will speak on "Administration—Hospital Pharmacy;" Dr. Charles Hartman, University of Georgia, Augusta, will cover "Past and Future Pharmacy Education;" and Dr. Clifton Lord, Southern College of Pharmacy, Atlanta, will speak on "The Responsibility of a Hospital Pharmacist."

President Jack Kirkland of Augusta, has announced two business sessions to be held on Wednesday, April 8, and Friday, April 10.

Tri-State Hospital Assembly

Plans have been announced for the Pharmacy Section Program of the Tri-State Hospital Assembly which will be held at the Palmer House in Chicago, April 27, 28, and 29. Sister Mary Cherubim, O.S.F., Chief Pharmacist at Saint Joseph Hospital in Joliet, Illinois, is currently serving as Chairman of the Section.

Papers scheduled for presentation during the three day session are as follows:

Monday, April 27—1:00-3:30 P.M.

Clinical and Pharmacological Review of Digitalis and Allied Drugs by Theodore Z. Polley, M.D., President, Illinois Heart Association.

The Status of Renal Pharmacology by Ralph W. Morris, Ph.D., Assistant Professor of Pharmacology, Department of Pharmacognosy and Pharmacology, University of Illinois.

Hematological Aspects of Drug Therapy by I. Schulman, M.D., Associate Professor of Pediatrics, Northwestern Medical School, Director of Hematology at Children's Memorial Hospital, Chicago.

Tuesday, April 28

Noon Luncheon—Relationship of the Hospital Pharmacist to the Poison Control Program by Joseph R. Christian, M.D., Professor, Department of Pediatrics, Stritch School of Medicine, and Chairman, Poisoning Control Committee, Illinois Chapter, American Academy of Pediatrics.

1:30-3:30 P.M.—Joint Session with Medical Record Librarians.

Reporting Drug Reactions by Irvin Kerlan, M.D., Associate Medical Director, Bureau of Medicine, Food and Drug Administration, Department of Health, Education and Welfare, Washington, D.C.

Panel Discussion—Hospital Administrator Meets Department Heads to Initiate Movement on Adverse Drug Reactions and Related Problems.

PANELISTS: Dr. Charles Letourneau, the Administrator-Moderator; Dr. Irvin Kerlan, Physician; Miss Norma Baumann, R.R.L., Medical Record Librarian; Sister M. Margaritis, P.H.J.C., R.N., Director of Nurses; Mrs. Robert Lee Leckrone, R.N., Nursing Service; and Mr. Louis Gdalman, R.Ph., Pharmacist.

Wednesday, April 29—1:30-4:40 P.M.

The Role of the Hospital Pharmacist in the Therapy of Water and Electrolytes by Harry F. Weisberg, M.D., Assistant Professor of Clinical Medicine, The Chicago Medical School, Chemical Pathologist, Little Company of Mary Hospital.

Inventory Control (Purchasing Procedures, Management, Standards) by Alfred A. Mannino, Sales Manager, Hospital Department, McKesson and Robbins, New York, N. Y.

Problem Session by a group of experts with representatives from four states.

Wisconsin Hospital Pharmacists to Sponsor Institute

Announcement has been made of plans for an institute to be sponsored by the Wisconsin Society of Hospital Pharmacists and presented by the Extension Services in Pharmacy of the University of Wisconsin. Meetings will be held on April 9 at the Wisconsin Center on the University of Wisconsin campus.

Speakers scheduled for the morning session include the following:

"Suggested Pricing Schedules for the Hospital Pharmacy," by Grover C. Bowles, Director, Department of Pharmacy, Baptist Memorial Hospital, Memphis, Tennessee.

"Narcotic Control in the Hospital Pharmacy," by Clifton J. Latiolais, Director, Pharmacy Service, University Hospital, Ohio State University, Columbus, Ohio.

"The Hospital Pharmacy and Its Responsibility in Hospital Accreditation," by Joseph Oddis, Staff Representative, American Hospital Association, Chicago, Illinois.

"The Hospital Formulary: Its Use and Importance to Hospital Pharmacy," by Don E. Francke, Director, Pharmacy Service, University Hospital, University of Michigan, Ann Arbor, Michigan.

The afternoon program will feature panel meetings of eight to ten hospital pharmacists each, who will discuss the questions previously listed by registrants on their registration forms. Each panel chairman will then report on the findings and recommendations of his panel to the entire group reassembled.

Reservations may be made through Richard S. Strommen, Extension Services in Pharmacy.

1959 Institutes Scheduled

The 1959 Institutes sponsored annually by the American Hospital Association in cooperation with the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS and the American Pharmaceutical Association, will be held at the University of Utah in Salt Lake City and at the University of Chicago, Chicago, Illinois. The Utah Institute is scheduled during the week of June 15 and the Chicago Institute during the week of August 3. The complete program and additional information will be published in a forthcoming issue of the JOURNAL. Also, all members of the ASHP will receive an announcement along with the necessary application forms.

Internship Program Announced

The Philadelphia College of Pharmacy and Science in cooperation with the Jefferson Medical College Hospital and Jefferson Medical College, and the Veterans Administration Hospital of Philadelphia, have announced plans for graduate instruction and residency program in hospital pharmacy administration. The cooperative program in hospital pharmacy administration has been designed to provide a practical educational program for persons with varying backgrounds and with varying professional aims and desires. The complete program of graduate instruction and residency will require a minimum of two academic years and the intervening summer.

The applicant must have been awarded a Bachelor of Science in Pharmacy degree from a School of Pharmacy accredited by the American Council on Pharmaceutical Education, have a superior academic record, be of good moral character, and in good health. The Graduate Committee, in selecting applicants for these courses, will consider their qualifications for a successful and creditable career as an administrative hospital pharmacist and will be guided by the information contained in the applications and in the letters of recommendation which they present. A personal interview may be required.

Applicants for the Veterans Administration Residency in Hospital Pharmacy must be registered as a pharmacist in one of the States or Territories of the United States, or in the District of Columbia prior to August 1 of the year for which application is made.

All successful applicants must take the qualifying examinations required of graduate students to be held early in September, annually, at the College of Pharmacy. If a student is found to have some undergraduate deficiency, he must be able to complete it in the academic year without infringing on the residency time.

For the program at Jefferson, the applicant should write to Dr. Louis A. Reber, Secretary, Graduate Committee, Philadelphia College of Pharmacy and Science, 43rd Street, Kingsessing and Woodland Avenues, Philadelphia 4, Pa., for the necessary application forms. This form, completed in duplicate, together with an official transcript of college work and three letters of recommendation from college professors, should be returned as soon as possible. Applicants will be selected in order of completion of their applications.

The Program with the Veterans Administration Hospital is conducted in accordance with the requirements established by the Administrator of Veterans Affairs and described in Announcement No. 97-B of the U.S. Civil Service Commission issued January 29, 1957. Interested persons are invited to write to the Secretary of the Graduate Committee as indicated above, or to the Central Board of U.S. Civil Service Examiners, Veterans Administration, Washington 25, D. C. for this announcement and necessary application forms.

as the president sees it—

ROBERT C. BOGASH, *Lenox Hill Hospital, New York City*

► ENROUTE TO AUSTIN, TEXAS, it was no accident that caused me to lay over in Houston for two days. The time was rewardingly spent visiting the American Operating Room Nurses' (A.O.R.N.) Convention.

I have a particular affinity for the A.O.R.N. Perhaps it is because I have had the pleasure of participating in a previous meeting and am now more aware of some of the myriad problems daily confronting O.R. nurses. Perhaps the closeness stems from our every day association in Lenox Hill Hospital as we approach a combined Pharmacy-Central Sterile Supply-Central Sterile Solutions Department. I suspect it is both of these combined with the impression I carried away from last year's meeting—that the A.O.R.N. is in many ways quite similar to the ASHP.

It is a young organization with idealistic goals. Their conventions are well attended by professional people who give undiluted attention to papers read, panel discussions, and scientific as well as professional exhibits. A.O.R.N. registrants listen avidly and question intelligently in their search for new techniques and refinements in procedures, instruments and equipment. Their basic drive is to learn more and share experiences in an effort to further improve their own practice through which better service is provided to the patient, surgeon and paramedical staff. As previously mentioned, there is much similarity between the A.O.R.N. and our own ASHP.

Your attendance at one of these meetings could be quite fruitful for you as well as your operating room personnel. Such exposure could give valuable insight to the peculiar problems that arise in handling, storing, sterilizing and administering medications in the O.R. You could become better acquainted with the instruments and equipment used in that department. There is a wealth of knowledge to be gained relative to sterile techniques, skin preps, emergency disinfection of 'dirty', contaminated, instruments and linen. All of which, once learned, helps make for expanded and better pharmacy service.

In fact, you need not wait to start with an A.O.R.N. Convention. A weekly visit to the operating room suites and anesthesiology department would be of great service if you did nothing but discuss the many new pharmaceutical agents being used in both the operating and recovery rooms. Once initiated, your visits will bring you into contact with current enigmas that can be resolved with good pharmacy counsel. A satisfying feeling is yours for the asking.

From Houston northward to Austin in Bob Lantos' new buckboard—out of Detroit was a Pontiac brand. The Seminar was excellent. Actually, I expected nothing less. Past experience has taught me that when you take one part interesting subject material, one part intense practitioners, one part good moderators, and one part attentive and inquisitive registrants, you have an almost infallible formula for a Seminar. And so it was.

Present were such notables as Leo Godley, Cedric Jeffers, Jim McKinley, who passed the presidential gavel to Guy Kelly, Adela Schneider, Clarence Henry, Dean Burlage, Dr. Lofgren, and the gracious Joe Arnette, newly elected Secretary of the Board of Pharmacy. I save for last the mention of our national 'veep' Cliff Latiolais who provided what proved for most of us unexpected excitement. During dinner Cliff received a message that Jayne had just increased the Latiolais census—with a son. Needless to say, Cliff exited happily, homeward bound.

Congratulations to both Cliff and Jayne.

Following the Seminar the next few days were spent in pleasant endeavors, namely the Visiting Guest Lecturer Series and enjoying the hospitality and table of Dean and Mrs. Burlage, Dr. and Mrs. Lofgren, and Mr. and Mrs. Arnette.

I must pay tribute to at least two of Dean Burlage's many facets. First, the Dean barbecues a marvelous steak. Second, the establishment of a farsighted, progressive, educational program called the Visiting Lecturer Series. Actually, the College of Pharmacy invites several speakers, each to present a series of three lectures. One lecture to junior and senior pharmacy students, the second to senior and graduate students who have enrolled for the Proseminar Course and lastly, to graduate students and faculty members. It has proved to be an exciting and rewarding program, I am told.

This is a fine approach to 'in training' education since it provides exposure to pharmacists and other professionals whose practice in other areas of the country may be different from that experienced locally. Again it permits exposure to undergraduates, graduates, and faculty which either singularly or collectively can generate interesting and, occasionally, provocative sessions.

I cannot help but note that I left the University of Texas College of Pharmacy with a wistful thought that more colleges of pharmacy initiate the progressive, educational program so artfully managed by Dean Burlage and his associate, Joe Arnette.

Throughout recent travels I have heard many compliments on The American Hospital Formulary Service. Practically every subscriber is pleased with the Service and what it embodies. Too, there have been a few complaints and even fewer criticisms. In most instances the complaints were minor and easily resolved. Of the criticisms, several were constructive and will be incorporated in the future editions of the Service. Still relative to censorials offered, to me at least, I am inclined to believe that most of them result from not completely realizing what the Formulary Services represents and how it should be utilized in the individual hospital. I suspect some of us expect the Formulary Service is a panacea in disguise. It is not. It is an extraordinary labor that, used properly, can save hundreds of hours and give a sense of uniform authority to information relative to pharmaceutical agents and supplies used in a given hospital. More it can not do—it remains for each of us to examine carefully the Formulary concept and then where desirable implement it by means of the best vehicle available—The American Hospital Formulary Service.

Robert C. Bogash—

SELECTED PHARMACEUTICAL ABSTRACTS

and summaries of other articles interesting to hospital pharmacists

. . . . . .

edited by CLIFTON J. LATIOLAIS, HENRY J. DEREWICZ *and* LEO F. GODLEY

IODIDE INCOMPATIBILITIES

Alkaloidal Iodides—Their Prescription Incompatibilities, Honkamp, L., Lichtin, J. L., Am. J. Pharm. 130:395 (Nov.) 1958.

The authors undertook a study of the incompatibilities of alkali metal iodides and hydriodic acid with certain alkaloidal salts. The alkaloids used were codeine phosphate and dihydrocodeinone bitartrate.

The studies indicated that when equal volumes of aqueous solutions of codeine phosphate and HI or KI were mixed, there was no precipitate of codeine iodide if the final mixture contained 130 mg. or less of the codeine salt mixed with 7.2 Gm. or less of KI, or 1.35 or less of HI, per 30 ml. There was also no precipitation in aqueous mixtures of dihydrocodeinone bitartrate and HI or KI if, in each 30 ml., there was 60 mg. or less of dihydrocodeinone mixed with 7.2 Gm. or less of KI or 1.35 Gm. or less of HI.

The tendency to form codeine iodide was lessened in the presence of the two cough proprietary mixtures studied (cheracol, Upjohn, and Mercodol, Merrell). It was determined that the more usual therapeutic concentrations of the alkaloids and the iodides did not form precipitates. The time at which precipitation occurs depends on the concentration of the ingredients. Hence the substances should be in as dilute a state as possible when mixing them. Alcohol in a 10% to 20% concentration inhibits the formation of a precipitate. There was no evidence to show that the higher alkalinity of potassium iodide solutions resulted in greater precipitation of the alkaloid than in the case of mixtures of HI and the alkaloid.

DOUGLAS SILVERNALE

CHEMICAL PREPARATIVE WORK IN A PHARMACY

On Some Possibilities of Chemical Preparative Work in the Laboratory of a Pharmacy, Barkovic D. and Ladanji N., Farmaceutski Glasnik (Yugoslavia) 14:559 (Dec.) 1958.

When studying the development of the preparation of chemical drugs in pharmacies, one observes a decreasing tendency to undertake this type of work, in contrast to the practice of former years. In comparison to preceding ones, present pharmacopeias thus contain very few monographs dealing with the direct preparation of chemical drugs the production of which is concentrated in the pharmaceutical industry today. However, the authors claim that even now there are very many opportunities for a pharmacist to work chemically in the pharmacy. Based on the experiences of a great pharmacy, they draw the pharmacists' attention to the following possibilities: (1) *Preparation of simple chemical drugs, e.g.* ammonium chloride, potassium chloride, quinine sulphate (starting from basic quinine or from unofficial quinine salts), sodium citrate, bismuth subgallate, potassium iodide, lead iodide, etc.; (2) *Regeneration of official chemical drugs.* It is possible to regenerate the following chemical drugs deteriorated by humidity, warmth, carbon dioxide and oxygen from the air, by means of recrystallization—copper sulphate, magnesium sulphate, sodium borate, sodium sulphate, zinc sulphate, etc: by means of drying in a drying box or in an exsiccator over sulfuric acid—ferric chloride, potassium carbonate, sodium iodide, sodium nitrite, pilocarpine hydrochloride, etc: by means of moderate heating—zinc oxide: by means of distillation—methylsalicylate, phenol, etc. (3) *Purification of technical chemical products* in order to obtain them in pharmaceutical purity. For example, technical boric acid, sodium sulphate, and sodium thiosulphate can be purified by crystallization from water whereas naphthalin by crystallization from alcohol; crude iodine can reach pharmaceutical quality after being sublimed. (4) *Preparation of some unstable chemical drugs,* for instance calcium acetylsalicylate (reaction between calcium carbonate and acetylsalicylic acid is to be used). (5) *Conversion of obsolete, deteriorated and not more active drugs* into other drugs or other modifications. From procaine-adrenaline tablets procaine hydrochloride can be isolated, from sodium dihydrocholate injections dihydrocholic acid can be obtained by due operations, etc. Especially useful is the possibility of isolating silver and gold from its colloidal compounds. (6) *Purification of chemicals to be used as reagents* in the control of drugs.

Although the experiences on the base of which these suggestions are made were collected in the activity of a large pharmacy, there are similar possibilities for such practices in smaller ones.

HUBERT ZACEK

STABILITY OF VITAMIN B_{12}

Stability of Vitamin B_{12}, Mukherjee, S. L. and Sen, S. P., J. Pharm. Pharmacol. 11:26 (Jan.) 1959 (Albert David Ltd., Calcutta.)

In an earlier investigation the authors had found that vitamin B_{12} activity is destroyed in the presence of a solution of aneurine (thiamine) and nicotinamide at a *p*H of 4 to 4.5. They had also found that aneurine alone destroyed vitamin B_{12} activity at a *p*H of 8.0. However, a solution of aneurine alone at *p*H of 4 to 4.5 did not cause deterioration of B_{12} at room temperature or at accelerated test conditions. The investigators had also found that the deterioration that did occur in the former instances could be satisfactorily prevented by the use of iron salts.

This led the authors to surmise that the decomposition products of aneurine and aneurine plus nicotinamide were not the same. Therefore, the effect of the decomposition products of these substances was further studied. Since vitamin B_{12} can be reduced by various reducing agents, the authors also investigated the reducing effect of both cysteine and hydrogen sulfide on vitamin B_{12}, as well as the protective effect of an iron salt, ferric chloride, in their presence.

Solutions of aneurine, nicotinamide, aneurine and nicotinamide, and cysteine and hydrogen sulfide were prepared and vitamin B_{12} was added to them. The solutions were then adjusted to a *p*H range of 4.5 to 8.0, the vials were capped and then the solutions were heated from 30 minutes to 4 hours. Iodimetric titrations were then performed to test the decomposition products for reducing agents, color tests for mercaptans were made and the microbiological potency of vitamin B_{12} was determined by the "Cup Plate Assay Method."

The solutions of cysteine and hydrogen sulfide inactivated the B_{12} as did the aneurine and nicotinamide solution. The solution of aneurine alone at a *p*H of 4.5 to 6.5 had little effect, but at a *p*H of 8.0 the B_{12} was inactivated. The solution of nicotinamide alone had little effect throughout the *p*H range of 4.5 to 8.0. When a solution containing decomposition product or products derived from heating aneurine solution alone at *p*H 8.0 was evaporated to dryness and the residue taken into solution, its titratable reducing properties were reduced as was its ability to destroy B_{12} activity. Furthermore, the evaporation of the solution liberated hydrogen sulfide.

It has been suggested that the thiazole moiety of aneurine is responsible for the destruction of vitamin B_{12}, and it has also been shown that aneurine in alkaline

releases an -SH group and with higher concentration of alkali finally decomposes into hydrogen sulfide. The initial decomposition product, therefore, is perhaps of a thiol nature, which on further heating decomposes into hydrogen sulfide. Ferric chloride in all cases offered protection against deterioration of the B_{12}.

ROBERT L. RAVIN

NEW TYPE SEDATIVE AND SOPORIFIC DRUG

New Type Sedative and Soporific Drug, Cronheim, G.; Gourzis, J. T.; and Toekes, I. M.; Science 128:1571 (Dec. 19) 1958. (Research Division, Riker Laboratories, Northridge, California).

Trimethoxybenzoyl-glycine-diethylamide induced in dogs and cats normal sleep without preceding ataxia. A five- to ten-fold increase of the soporific dose resulted in restlessness and disorientation instead of sleep. In man, oral doses of 500 to 1500 mg. caused sedation or drowsiness, or both, in half the cases. No spindling or drug-induced artifacts were found in electroencephalographic recordings.

AUTHOR'S SUMMARY

STABILIZATION OF INJECTABLE SOLUTIONS

Stabilization of Injectable Solutions, Prozorovskiy A. S. and Kudakova N. A., Aptechnoe Delo (U.S.S.R.) 7:44 (Nov.-Dec.) 1958.

When preparing injectable solutions of salts of many alkaloids, *e.g.* apomorphine, arecoline, atropine, cocaine, morphine, papaverine, scopolamine, strychnine, eserine etc., and related nitrogenous bases it has become a common practice to add hydrochloric acid to prevent formation of precipitates or decomposition of the above mentioned substances. The amount of hydrochloric acid required for this stabilization varies according to different authors between 3 ml. and 20 ml. of 0.1 N hydrochloric acid for 1 liter of solution. This corresponds to the limits of pH of 3.52 to 2.57 respectively. However, there have been found contradictions in the many suggestions for the preparation of injectable solutions of the aforesaid substances. It therefore is necessary to elaborate standard instructions to be respected when preparing these solutions. The stabilization of injectable solutions for peridural and cerebrospinal anesthesia needs particular consideration as these solutions should not have a pH lower than 5 whereas the solutions of procaine with the addition of hydrochloric acid which are used for the above named purpose are characterized by a pH of 4.2 - 4.5. Finally, elaborating of a table with standard instructions for sterilization is called for.

HUBERT ZACEK

DETERMINATION OF HEAT STABILITY OF MEDICINAL WHITE OILS

Determination of Heat Stability of Medicinal White Oils, Salzmann, L., J. Am. Pharm. Assoc., Sci. Ed. 47:885 (Dec.) 1958. (L. Sonneborn Sons, Inc., New York 10, N.Y.

The author describes a simplified procedure to determine the expected shelf life of medicinal white oil. In demonstrating this method, the author describes the U.S.P. method which he has used considerably but which has many disadvantages in that the official tests sometimes give erroneous results caused by either trace impurities in the test tubes used or an oversensitivity of the test solution. Thus a high quality oil might be discarded. In the new procedure, however, a single oil sample is heated and tested for the presence of hydroperoxides at definite time intervals by a rapid spot test carried out on filter paper. The heating time required for hydroperoxides to form in the oil, as observed visually by the development of a pink color on the filter paper, indicates the stability of the oil.

HENRY J. DEREWICZ

STABILITY OF POSTERIOR PITUITARY INJECTIONS

The Stability of Posterior Pituitary Injections During Storage, Nielsen, A. T., Dansk Tidsskrift for Farmaci 33:1 (Jan.) 1959. (Royal Danish School of Pharmacy, Laboratory of Pharmaceutical Biology, Copenhagen).

The stability of a Posterior Pituitary Injection prepared from an acetone-desiccated powder of the posterior pituitary glands of swine was studied. The solution was stored at different temperatures ranging from ca. 5°C. (refrigerator) to 50°C. Samples were assayed at intervals for oxytocic activity (rat's uterus) and pressor activity (rat's blood pressure). The influence of the hydrogen ion concentration at ca. 5°C. and 22.5°C. is shown in Fig. 1. Data from earlier experiments at 116°C. (Nielsen) are plotted in Fig. 5. These experiments, when compared with experiments by Gerlough, suggest that the stability optimum with increasing temperature shifts towards a more acid reaction. The optimum pH for storage at low temperature cannot, therefore, be deducted from accelerated storage experiments at elevated temperatures (about 100°C.).

The results from these and earlier experiments (Nielsen) are combined in Fig. 4. The velocity constants (k) are calculated from eq. (I), p. 4, when the time (t) is in years. If the results agreed with Arrhenius' Law, eq. (II), p. 4, one should expect a straight line when $\log_{10}k$ was plotted against the reciprocal absolute temperature (1/T). The data in question, however, are fitting a straight line better when the temperature is used directly as abscissa. By extrapolation Fig. 4 is used to estimate the reaction velocity at lower temperatures. At such low temperatures the rate of inactivation is so small that it is hardly possible to demonstrate any inactivation during the experimental period.

From the experiments can be calculated that the injection with a maximum loss of 5% of the activity can be stored as follows:

Refrigerator:	3 - 4 years
6-15°C.:	1 year
15-20°C.:	6 months

It can be concluded that Posterior Pituitary Injection should be kept in refrigerator as recommended in the *British Pharmacopoeia.*

AUTHOR'S SUMMARY

COMPRESSION OF CRYSTALLINE SUBSTANCES

Compression of Crystalline Substances, Jaffe, J., Foss, N.F.; J. Am. Pharm. Assoc., Sci. Ed., 48:26 (Jan.) 1959. (Univ. of Maryland).

An attempt has been made to clarify the role played by various properties and characteristics of crystals, and the ability of these crystals to form tablets when subjected to direct compression. The relationship of crystal structure to molecular structure was investigated, and this relationship applied to possible physical properties, primarily that property of tablet formation on direct compression.

This study did not attempt to correlate the feed properties nor were the factors of sticking, picking, chipping, capping considered in the ability of the substances to form tablets under direct compression. A Stokes Eureka A-3 single punch tablet machine, manually operated, was employed. A flat-head, 7/16 inch punch was used in all cases. Substances were considered unsuitable if they did not resist pressure of 5 Kg. or less on a Strong-Cobb Hardness Tester.

The crystal system, binary compounds, water of crystallization, boiling point, carbonate radical, sulfate radical, and substances forming structurally neutral layer latices were found to influence tablet formation.

J. A. OLIVER

INTERACTIONS BETWEEN QUATERNARY AMMONIUM COMPOUNDS AND SEVERAL CERTIFIED DYES

Interactions Between Quaternary Ammonium Compounds and Several Certified Dyes, Lachman, L.; Kuramoto, R.; Cooper, J., J. Am. Pharm. Assoc., Sci. Ed. 47:871 (Dec.) 1958. (From Research Labs, Ciba Pharm. Products, Inc., Summit, N.J.)

The authors demonstrate that when solutions of quaternary ammonium compounds and certified dyes are prepared, a precipitation or clouding results in several of these solutions. The authors performed a phase study between several quaternary ammonium compounds and dyes to determine the concentration relationships needed to cause precipitation of the reacted species. Phase diagrams are presented for the systems cetylpyridinium chloride-dye, benzalkonium chloride-dye, and dodecyldimethyl (2-phenoxyethyl) ammonium bromide dye. Three certified dyes, D & C yellow No. 10, FD & C Red No. 1, and FD & C Blue No. 1 were used with each quaternary ammonium compound. These phase diagrams indicate the areas of physical compatability and incompatibility. Among the most important results of this study are the following:

1. Cetylpyridinium chloride, benzalkonium chloride, and dodecyldimethyl (2-phenoxyethyl) ammonium bromide were found to form insoluble complexes with FD & C Red No. 1, FD & C Blue No. 1, and D & C Yellow No. 10.

2. For any given quantity of the quaternary ammonium compound, the region of miscibility will increase in the following order: benzalkonium chloride, dodecyldimethyl (2-phenoxymethyl) ammonium bromide, and cetylpyridinium chloride.

HENRY J. DEREWICZ

TABLET COLOR COATING WITH PIGMENTS

Tablet Color Coating with Pigments, Tucker, S. J.; Nicholson, A. E.; and Engelbert, H., J. Am. Pharm. Assoc., Sci. Ed. 47:849 (Dec.) 1958. (From Smith, Kline and French Labs, Philadelphia, Pa.)

The authors describe a new method for coloring sugar-coated tablets using pigments rather than water-soluble dyes. Because the economics of present industrial methods demand lower costs in tablet coating coupled with an increasing difficulty in choosing a tablet color which is distinctive and yet has sufficient light-stability, the use of pigments, water-insoluble D & C dyes, or D & C lakes suspended with titanium dioxide in syrup overcomes the shortcomings of present methods of coloring. The authors indicate that the new method allows: 1. coating applications immediately following the rounding coats, in many cases thereby eliminating the smoothing coats. 2. A reduction in time and number of coats required to apply the coloration. 3. An easy matching of colors from lot to lot. 4. A new and different number of color shades. 5. Excellent light stability. Mention is also made of the fact that tablets cannot be overcolored. The authors also present tables indicating the light stability of the color dyes and lakes. The authors also offer the stock suspension formula, below, for applying the pigment to the rounded tablets:

Purified Water	250.00 ml.
Dioctyl sodium sulfosuccinate	0.01 Gm.
D & C. lake or D & C water-insoluble dye	1-15.00 Gm.
Titanium dioxide	100.00 Gm.
Syrup U.S.P.	500.0 ml.

The above suspension is combined with syrup to form the coating suspension used by the authors in the following ratio:

Stock suspension	100.00 Gm.
Coating Syrup, to make	500 ml.

HENRY J. DEREWICZ

ERYTHROMYCIN IN VARIOUS SUPPOSITORY BASES

A Comparison of the Antibacterial Activity of Erythromycin in Various Suppository Bases, Blissitt, C. W., Disseration Abstracts 19:1059 (Nov.) 1958.

Suppositories containing 50 mg. erythromycin were tested for antibacterial activity by the agar cup-plate FDA method. The following bases were used: (a) cocoa butter, (b) cocoa butter with one percent aerosol O.T., (c) Carbowax 1500 and 4000, equal parts, and (d) polyoxyethylene stearate with three percent white wax and five percent water. All suppositories exhibited antibacterial activity over a five month period with the Carbowax base being the most effective. The erythromycin suppositories were found stable in all bases except the one containing polyoxyethylene stearate, where loss of activity was noted at the end of one month storage.

NORMAN HO

ASSAY OF PROMAZINE

Assay of Promazine and its Separation from Chlorpromazine and Promethazine, Cavatorta, L., J. Pharm. and Pharmacol. 11:49 (Jan.) 1959. (Analytical Dept., Lepetit S.p.A., Milan, Italy.)

The author describes a colorimetric method to identify and quantitatively determine promazine, in pharmaceutical preparations. The method is applicable to promazine and promethazine mixtures, and promazine and chlorpromazine in mixtures. With a second colorimetric method, promethazine or promethazine in the presence of the other two substances can be determined. Briefly, the assay is based upon the assay of phenothiazine by the formation of a complex with palladium chloride and also in the fact that promethazine differs from chlorpromazine in having a substituted isopropyl instead of a propyl group. Promethazine may be differentiated from the two other products using mercuric sulfate as reagent, which besides acting as an oxidizing agent is also used to detect isopropanol in the presence of propanol. The author also presents various tables showing colors and wavelengths used in determining promazine, promethazine and chlorpromazine.

HENRY J. DEREWICZ

EFFECT OF CLOSURES ON STABILITY

Stability of Aqueous Solutions in Ampoules and Multiple-dose Containers Closed by Means of Polyvinyl Chloride or Rubber Caps, Nielsen, A. B., Dansk. Tidsskr. Farm. 32:109, 1958.

A number of solutions were stored in ampoules, vials closed with rubber caps, and vials closed with "resistant caps" made from polyvinyl chloride backed with rubber. Solutions of sodium aurichloride and potassium permanganate were shown to be most rapidly reduced in the vials closed with rubber caps, and during six months' storage ascorbic acid solutions decomposed to the greatest extent in contact with the rubber caps. In experiments with solutions of adrenaline and sodium nitrite little difference was observed between rubber and polyvinyl chloride caps. "Resistant" caps absorb sodium metabisulphite to a smaller extent than rubber caps, and seem preferable for many solutions. However, they absorb phenol and chlorocresol more readily than rubber caps, and so cannot be recommended for use in the presence of phenolic bacteriostatics.

AUTHOR'S SUMMARY

CURRENT LITERATURE

. . . also calling your attention to the following articles appearing in recent hospital and pharmaceutical journals

. . . . . .

DISPENSING

Lantos, R. L.: Drug Distribution is the Pharmacy's Job, *Modern Hosp.* 92:104 (Feb.) 1959.

DRUG SAMPLES

Anon.: Drug Samples and Hospitals, *Am. Profess. Pharm.* 25:46 (Jan.) 1959.

EQUIPMENT AND APPARATUS

Whittet, T. D.: Methods of Purifying Water for Pharmaceutical Purposes, *Public Pharmacist* (Great Britain) 16:33 (Jan.) 1959.

FORMULARY SYSTEM

Editorial:Reviewing the Formulary, *Hospitals* 32:25 (Feb. 1) 1959.

NARCOTICS

Anon.: Verbal Prescriptions for Narcotics, *Am. Profess. Pharm.* 25:48 (Jan.) 1959.

OPHTHALMIC SOLUTIONS

Tozer, G. A.: Ophthalmic Solutions, *Am. Profess. Pharm.* 25:30 (Jan.) 1959.

OUTPATIENT PRESCRIPTIONS

Parker, Paul F.: Retail Pharmacy and Outpatient Prescriptions, *J. Am. Pharm. Assoc., Pract. Pharm. Ed.* 20:96 (Feb.) 1959.

PROFESSIONAL AND PUBLIC RELATIONS

Archambault, G. F.: Pharmacy Human Relations, *Hosp. Progress* 40:83 (Feb.) 1959.

PURCHASING

Sister M. Bernadine Wild: Purchasing Disposables—A Survey (concluded from article appearing in January issue) *Hosp. Progress* 40:110 (Feb.) 1959.

DRUG EVALUATIONS

by the Council on Drugs of the American Medical Association

► THE FOLLOWING MONOGRAPHS and supplemental statements on drugs have been authorized by the Council on Drugs of the American Medical Association for publication and inclusion in *New and Nonofficial Drugs*. They are based upon the evaluation of available scientific data and reports of investigations. In order to make the material even more valuable, dosage forms and preparations of individual drugs have been added to the monographs. These dosage forms and preparations were not taken from material published in the *Journal of the American Medical Association* by the Council on Drugs; rather, they were obtained from such manufacturers' brochures, news releases, etc., which were available to us at the time of publication. An attempt has been made to make the list of dosage forms as complete as possible. However, no guarantee can be made that the list of preparations is complete and it is suggested that hospital pharmacists consult manufacturers' releases for additional dosage forms and preparations.

The issues of the *Journal of the American Medical Association* from which each monograph has been taken is noted under each monograph. Monographs in this issue of the JOURNAL include those published in the *Journal* to Jan. 24, 1959.

Notice

New and Nonofficial Drugs 1959 is now available from your local bookstore and from the publishers, J. B. Lippincott Company, Philadelphia, Pa. This 1959 edition contains monographs of drugs evaluated by the Council on Drugs of the American Medical Association and published in the Journal of the A.M.A. to January 1, 1959. The index listed below contains those drugs evaluated and published between December 20, 1958 and January 24, 1959.

Index

TO DRUGS EVALUATED IN THIS ISSUE

page

141 ADRENAL DISORDERS, Current Status of the Treatment of
141 ADRENAL STEROID HORMONES
140 ARISTOCORT
140 DARTAL HYDROCHLORIDE
139 FURAZOLIDONE
139 FUROXONE
140 KENACORT
141 STEROID HORMONES
140 THIOPROPAZATE HYDROCHLORIDE
140 TRIAMCINOLONE

Index

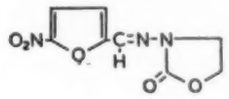
TO EVALUATED DRUGS IN THE FEBRUARY 1959 ISSUE OF THE AMERICAN JOURNAL OF HOSPITAL PHARMACY.

page

96 ACETYL SULFAMETHOXYPYRIDAZINE
95 KYNEX
96 KYNEX ACETYL
95 MIDICEL
94 NICOTINIC ACID, Use of in Hypercholesteremia
92 ORAL MEDICATION with Preparations for Prolonged Action
95 RABIES VACCINE (Duck Embryo)
95 SULFAMETHOXYPYRIDAZINE
96 TRIFLUPROMAZINE HYDROCHLORIDE
96 VESPRIN

Furazolidone — Furoxone ®

FURAZOLIDONE is 3-(5-nitro-2-furfurylideneamino)-2-oxazolidinone.—The structural formula of furazolidone may be represented as follows:



Actions and Uses

Furazolidone, a nitrofuran derivative, shows antibacterial activity in vitro against a variety of gram-negative and gram-positive enteric organisms, including species of Salmonella, Shigella, Escherichia, Proteus, Streptococcus, and Staphylococcus. It also shows antiprotozoal activity and has been incorporated in combination with other topical preparations for the treatment of trichomonal infections of the vagina. The precise mechanism of action of furazolidone is not fully understood, but the drug is believed to act by inhibiting dehydrogenase systems of the microbial cell.

Orally administered furazolidone is proposed for the treatment of bacterial diarrheal disorders and enteritis. Its usefulness for the foregoing purposes is based on subjective observations in a relatively small number of cases. Since many bacterial diarrheas are self-limited and of short duration, it is difficult to determine what part in the over-all clinical improvement of the patient might be ascribed to the action of the drug. Nevertheless, it is the clinical impression of observers that furazolidone is useful in the treatment of some patients with acute bacterial gastrointestinal upsets. The drug apparently is capable of arresting some infections due to strains of bacteria which are resistant to the usual antibiotics. Although well-controlled clinical studies are needed to establish its ultimate efficacy, furazolidone shows promise as a chemotherapeutic agent for bacterial enteritis and diarrhea.

In the clinical trials thus far, nausea and vomiting seem to be the most frequent side-effects to orally administered furazolidone. These symptoms usually subside upon reduction in dosage. In occasional patients, headache has been observed. A few patients have shown sensitization reactions in the form of a vesicular or morbilliform pruritic rash. This has disappeared upon cessation of treatment. Hypochromic anemia has been observed occasionally after long-term therapy, but it is not certain whether this effect is due to

dietary factors rather than to the drug. Overgrowth of nonsusceptible organisms with resulting colitis, proctitis, anal pruritus, and monilial or staphylococcic enteritis has not been observed. There are no known absolute contraindications to the administration of furazolidone.

Dosage

Furazolidone is administered orally. The usual dose for adults is 100 mg. four times daily. For children five years of age or older, the dose is 50 mg. four times a day. Dosage for children between 1 and 5 years of age is 25 to 33 mg. four times daily. For infants up to one year of age, 8 to 16 mg. is given four times a day. The maximum daily dose for adults and children should not exceed 7.5 mg. per kilogram of body weight, given in four divided doses over a period of 24 hours.

Preparations: suspension (oral) 3.33 mg. per cc.; tablets 100 mg.
Applicable commercial name: Furoxone.
Eaton Laboratories cooperated by furnishing scientific data to aid in the evaluation of furazolidone.
***J. Am. Med. Assoc. 169*:135/255 (Jan. 17) 1959.**

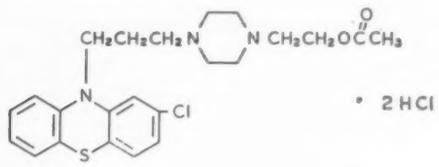
Preparations

Suspension, Oral, Furazolidone (Furoxone) 50 mg. per 15 ml., with kaolin and pectin; 240 ml. bottles.
Tablets Furazolidone (Furoxone) 100 mg.

Thiopropazate Hydrochloride

Dartal ® Dihydrochloride

THIOPROPAZATE HYDROCHLORIDE is 2-chloro-10-{3-[4-(2-acetoxyethyl)piperazinyl]propyl}phenothiazine dihydrochloride.—The structural formula of thiopropazate hydrochloride may be represented as follows:



Actions and Uses

Thiopropazate hydrochloride is a phenothiazine derivative with actions and uses similar to those of other agents of this type. Chemically and pharmacologically, it is most closely related to prochlorperazine and perphenazine. Thiopropazate is a potent compound, and it produces comparable pharmacological effects with doses that are considerably less than those of chlorpromazine. It has a spectrum of clinical usefulness akin to that of other phenothiazine derivatives and is subject to similar limitations. Available clinical evidence, although not well controlled, would indicate that the principal clinical application of thiopropazate will be in the management of psychoses in which agitation, tension, combativeness, and aggressiveness predominate. The drug is apparently capable of eliciting beneficial responses in some patients who fail to respond to other closely related compounds. It is also of value in some patients with psychomotor retardation, apathy, and lethargy. Animal experiments have shown that the drug possesses potent antiemetic properties, but it has not been evaluated clinically for this purpose.

Certain typical phenothiazine side-effects such as sedation and hypotension have been reported to be less frequent and less severe with thiopropazate than with other agents of this class, particularly chlorpromazine. Although the drug has produced leukopenia, no cases of granulocytopenia have been recorded to date. Likewise, jaundice has not occurred during its clinical trial. In view of the phenothiazine structure of thiopropazate, however, such untoward reactions should be watched for. The most frequent and troublesome side-effect of this drug has been Parkinson-like symptoms referable to extrapyramidal involvement. Tremors, rigidity, fixed facies, and drooling frequently complicate therapy with this agent. Although such neurological effects appear to be a function of dosage, there is a very narrow range between clinically effective doses and those causing extrapyramidal symptoms.

The usual contraindications to phenothiazine derivatives in general apply to thiopropazate and include patients with severe depressions, those with liver damage, and persons under the influence of other central nervous system depressants. The drug should not be given to patients with convulsive disorders.

Dosage

Thiopropazate hydrochloride is administered orally in doses which must be individualized according to the severity of the condition under treatment, the response of the particular patient, and the appearance of side-effects.

For the management of patients with psychotic conditions, the usual initial dose is 10 mg. three times a day. This dose is then adjusted upward or downward in daily increments of 10 mg. given at intervals of three or four days, according to therapeutic response. At present, 100 mg. per day should be considered a maximum dose. For anxiety tension states, psychosomatic conditions, and other neuroses, the foregoing dosage schedule is reduced by half.

Preparations: tablets 5 mg. and 10 mg.
Applicable commerical name: Dartal Dihydrochloride.
G. D. Searle & Co. cooperated by furnishing scientific data to aid in the evaluation of thiopropazate hydrochloride.
***J. Am. Med. Assoc. 169*:136/256 (Jan. 17) 1959.**

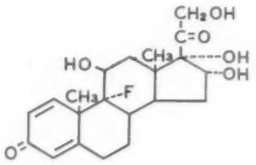
Preparations

Tablets Thiopropazate (Dartal) Hydrochloride 5 mg. and 10 mg.

Triamcinolone

Aristocort ®
Kenacort ®

TRIAMCINOLONE is 9α-fluoro-16α-hydroxyprednisolone.—The structural formula of triamcinolone may be represented as follows:



Actions and Uses

Triamcinolone is a potent glucocorticoid with anti-inflammatory, hormonal, and metabolic effects similar to those of prednisolone. It has an anti-inflammatory potency greater than that of an equal amount of prednisolone, i.e., comparable suppressive effects may usually be achieved with lower doses of triamcinolone than with prednisolone. Triamcinolone lacks the sodium-retaining and edema-producing effects of most other glucocorticoids. During the first several days of administration, it may cause a loss of sodium from the body; an initial mild diuretic action is frequently observed, whether the patient is frankly edematous or not.

This is in contrast to the definite sodium-retaining and fluid-retaining properties of cortisone and hydrocortisone and to a much lesser extent with prednisone and prednisolone. Except in exceedingly large doses, triamcinolone apparently has no consistent effect on potassium excretion. Hence, neither sodium restriction nor potassium supplementation is ordinarily required during therapy with this agent. As with other glucocorticoids, the long-term administration of triamcinolone results in definite catabolic effects, as indicated by impairment of carbohydrate utilization and negative protein and calcium balance. This catabolic effect, coupled with a lack of appetite stimulation which is apparently peculiar to triamcinolone, may produce weight loss that might be undesirable in some patients treated for long periods of time. However, the voracious appetite, with weight gain and euphoria, characteristic of other steroids, is not seen with administration of triamcinolone.

Triamcinolone has been used for the management of a wide variety of clinical conditions usually considered amenable to systemic steroid therapy. These have included rheumatoid arthritis and other collagen diseases, allergic and dermatological disorders, certain leukemias and malignant lymphomas, the nephrotic syndrome, pulmonary emphysema and fibrosis, acute bursitis, rheumatic fever, and certain blood dyscrasias. Although clinical experience with the drug in some of the foregoing conditions is not extensive, the many similarities in action between triamcinolone and other potent glucocorticoids would indicate a usefulness for triamcinolone akin to that of other agents of this class. There is some evidence that triamcinolone is more effective at a smaller dosage than are other steroids in controlling both the skin and the joint lesions in psoriasis, whether or not complicated by arthropathy. Because it does not exert strong mineralocorticoid effects, triamcinolone is probably not as effective as cortisone or hydrocortisone for the management of acute adrenal insufficiency. Triamcinolone appears to compare favorably with other steroids for use in those situations in which edema and sodium retention have been complicating problems. It may also be the steroid of choice for patients in whom psychic stimulation, euphoria, voracious appetite, and weight gain should be avoided. Like all other hormones of this type, triamcinolone suppresses, but does not cure, the manifestations of the various diseases treated.

Although electrolyte imbalance rarely complicates therapy with triamcinolone, the drug does produce the other side-effects and untoward reactions common to the glucocorticoids. At therapeutically equivalent doses, the frequency and severity of clinical manifestations of hyperadrenalism—rounding of the face, fat deposition, and hirsutism—are essentially the same. Likewise, there is little indication that the relative incidence of osteoporosis is materially decreased after the long-term use of the drug. Triamcinolone apparently does not cause the euphoria sometimes seen with other steroids, and the occurrence of mental depressions is uncommon. Current evidence suggests that the drug may not produce as high an incidence of peptic ulcer as do other steroids. Cutaneous erythema seems to be a side effect peculiar to triamcinolone. The usual contraindications and precautions of glucocorticoid therapy should be followed in the use of triamcinolone, keeping in mind that prolonged therapy with this drug will suppress the function of the patient's own adrenals by interfering with the pituitary-adrenal axis.

Dosage

Triamcinolone is administered orally. Dosage varies with the condition being treated, its severity, appearance of side-effects, and individual response. For the common diseases amenable to systemic steroid therapy, the usual initial (suppressive) dose for adults ranges from 8 to 20 mg. per day in three or four divided doses. When a satisfactory response is obtained, the initial dose is reduced gradually in decrements of 2 mg. every two or three days until a maintenance dosage level is reached which will adequately maintain the patient's condition. For the treatment of rheumatoid arthritis, the necessity of large initial doses, with subsequent step-wise reduction to maintenance levels, has been questioned by some authorities who favor, instead, the initiation of therapy with doses believed to be the eventual maintenance dose.

Preparations: tablets, 1 mg., 2 mg. and 4 mg.
Applicable commercial name: Aristocort, Kenacort.
Lederle Laboratories Division, American Cyanamid Company, cooperated by furnishing scientific data to aid in the evaluation of triamcinolone.

J. Am. Med. Assoc. 169:137/257 (Jan. 17) 1959.

Preparations

Tablets Triamcinolone (Aristocort; Kenacort) 1 mg., 2 mg., and 4 mg.

CURRENT STATUS OF THE TREATMENT OF ADRENAL DISORDERS

Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations.

H. D. KAUTZ, M.D., *Secretary*

GEORGE W. THORN, M.D., DON H. NELSON, M.D. *and* ALBERT E. RENOLD, M.D., BOSTON

► THE AVAILABILITY of precise diagnostic techniques and the synthesis of several important adrenal cortical steroids provide the practicing physician with an unusual opportunity for establishing a correct diagnosis and initiating appropriate therapy in patients with abnormalities of adrenal cortical function. The ever-widening horizon of the non-specific use of adrenal steroid therapy and the exploration of the beneficial effect of hypophysectomy and adrenalectomy have increased greatly the numbers of patients with evidence of altered adrenal cortical function. The development of accurate and clinically applicable measurements of catechol amine levels in blood and urine has enhanced the accuracy with which pheochromocytoma may be detected and has provided a new and important screening technique which should be applied to all patients with hypertension of undetermined origin.

From the departments of medicine, Harvard Medical School and the Peter Bent Brigham Hospital (Drs. Thorn, Renold, and Nelson) and investigator, Howard Hughes Medical Institute (Dr. Nelson).

Hormone Preparations

The structural formulas of the adrenal steroid compounds are represented in figure 1.

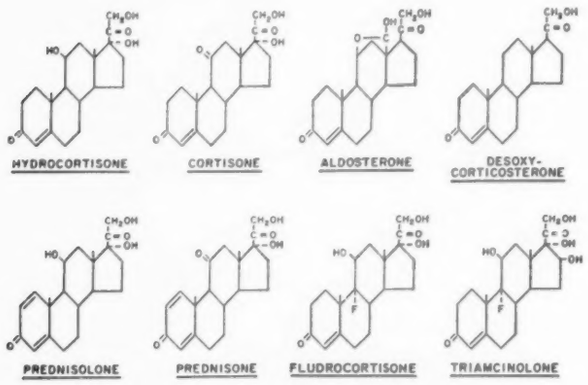


Fig. 1.—Steroid hormone preparations.

Corticotropin.—Corticotropin (Acth, Lyophilized Acthar, Corticotropin, Lyophilized Corticotropin), also known as ACTH, adrenocorticotrophin, and corticotrophin, is available as a lyophilized powder, containing 10 to 40 U.S.P. units per vial for intravenous infusion or for intramuscular injection when dissolved in saline solution. Corticotropin is also available as a solution in gelatin, containing 20 to 100 "clinical units" per cubic centimeter, or in combination with zinc as corticotropin-zinc hydroxide (Cortrophin-Zinc) for intramuscular administration only. These preparations provide prolonged activity (18 to 36 hours) after a single intramuscular injection. "Clinical units" are equivalent approximately to one-third U. S. P. units. A U. S. P. unit equals 1 I. U., which, in turn, represents the biological activity of 1 mg. of corticotropin International Standard, as determined by measurement of the adrenal ascorbic secretion in the hypophy-sectomized rat.

In diseases of adrenal origin the use of corticotropin is confined largely to diagnostic procedures and for stimulating the adrenal cortex after prolonged steroid therapy. The administration of corticotropin, given intramuscularly and particularly intravenously, may precipitate a crisis in a patient with adrenal cortical unresponsiveness unless the patient is protected by the simultaneous administration of a cortisone-like steroid.

Cortisone-like Steroids.—The cortisone-like steroids, also known as 17-hydroxysteroids, are listed as follows.

Hydrocortisone (Cortef, Cortisol, Cortril, Hycortole, Hydrocortone): Hydrocortisone is available in solution in 50% ethyl alcohol, 100 mg. per 20 cc., and as hydrocortisone sodium succinate (Solu-Cortef), 134 mg. of this compound being equivalent to 100 mg. of hydrocortisone for intravenous or intramuscular injection. It is also available as the acetate in saline suspension for intramuscular use (25 mg. per cubic centimeter) and as 20-mg. tablets for oral use. Hydrocortisone, especially the succinate ester, is the only preparation available for immediate and rapid intravenous use. Conversely, the absorption of hydrocortisone acetate after intramuscular injection is much slower than cortisone and hence should be used only when a prolonged effect from a single injection is desired.

Cortisone (Cortisone, Cortogen, Cortone): Cortisone is available as the acetate in saline suspension (25 and 50 mg. per cubic centimeter) for intramuscular use and in tablets for oral use (5, 10, and 25 mg.). For all practical purposes cortisone and hydrocortisone are equivalent milligram for milligram.

Prednisone (Deltasone, Deltra, Meticorten) and prednisolone (Delta Cortef, Hydeltra, Meticortelone): Prednisone and prednisolone are available as 2.5-mg. and 5-mg. tablets for oral use. One milligram of prednisone or prednisolone is equivalent to 4 to 5 mg. of cortisone or hydrocortisone. Prednisone and prednisolone exert much less sodium-retaining effect, milligram for milligram, than does cortisone or hydrocortisone.

Triamcinolone (Aristocort, Kenacort): Triamcinolone is available as 4-mg. tablets for oral use. One milligram of triamcinolone is equal to approximately 6 mg. of cortisone or hydrocortisone. This substance, milligram for milligram, possesses even less sodium-retaining effect than does prednisone or prednisolone.

Fludrocortisone (Alflorone, F-Cortef, Florinef): Fludrocortisone is available as the acetate in 0.1-mg. and 1.0-mg. tablets. This derivative of hydrocortisone is approximately 25 times as active as cortisone, hydrocortisone, and desoxycorticosterone (Cortate, Decortin, Decosterone, Doca, Percorten); hence, its sodium-retaining action is very great in relation to its cortisone-like action.

Sodium-Retaining Adrenal Steroids.—All adrenal steroids are "sodium-retaining" to some extent under normal conditions. However, unless very large doses of cortisone, hydrocortisone, and prednisone are employed, this activity is not prominent.

Fludrocortisone: Fludrocortisone, as noted previously, is an extremely active sodium-retaining hormone, 1 mg. by mouth being equivalent to 25 mg. of desoxycorticosterone given by injection.

Desoxycorticosterone: Desoxycorticosterone is available for intramuscular injection as the acetate in sesame oil (5 mg. per cubic centimeter). For prolonged effect (15 to 30 days), it is available as a suspension of the trimethylacetate ester (25 mg. per cubic centimeter) and as the acetate in 2-mg. and 5-mg. buccal tablets for sublingual use.

Aldosterone: Aldosterone, the naturally occurring sodium-retaining hormone in man, is not available commercially.

Special Considerations.—The high potency of fludrocortisone, in respect to both its cortisone-like effect and its sodium-retaining effect, makes the administration of this substance particularly advantageous when adrenocorticotropin tests are being carried out. Patients with suspected Addison's disease can be given 1 to 2 mg. of this substance daily while the tests are being conducted, without concern for the hormone derived from this substance which may appear in the urine, since the quantity is so small. Furthermore, larger doses of this substance may be substituted in patients on prolonged cortisone therapy in whom it is desirable to test reserve adrenal capacity before hormone therapy is reduced or discontinued. Thus, 4 to 5 mg. of fludrocortisone is equivalent to 100 mg. of cortisone or hydrocortisone. However, the dietary sodium should be rigidly restricted during the period of substitution to avoid excessive sodium retention. Supplementary potassium chloride (3 to 6 Gm. daily) may also be given.

Acute Adrenal Crisis

Such an emergency may be precipitated in a patient with chronic adrenal cortical insufficiency by the superimposition of stress, such as intercurrent infection, surgery, or trauma. It may also be precipitated in patients on long-term, large-dosage cortisone therapy by the sudden withdrawal of hormone therapy or by the superimposition of stress without an accompanying increase in steroid therapy. Acute adrenal crisis may occur as a complication of anticoagulant therapy (hemorrhage into the adrenal gland) or may present itself as shock in conjunction with surgery, hemorrhage, or acute infection. It is nearly always impossible to establish with certainty the diagnosis of acute adrenal crisis at the time a patient presents the picture of acute hypotensive shock.

Blood is drawn, if possible, for serum steroid determination, and 100 mg. of hydrocortisone sodium succinate, given

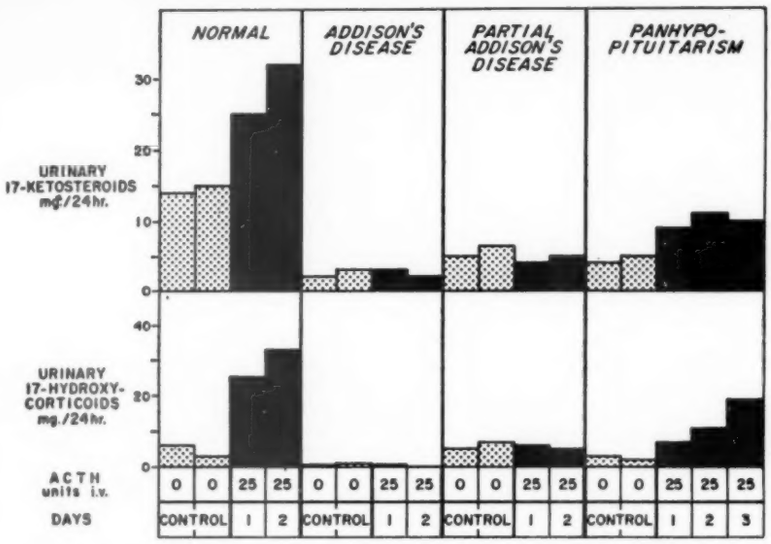


Fig. 2.—Response to intravenously given corticotropin in adrenal insufficiency.

intravenously, is administered immediately. This procedure may be life-saving. Pressor amines should be used in conjunction with hydrocortisone in an effort to maintain blood pressure. The use of whole blood, plasma, or albumin and electrolyte solutions given intravenously will be dictated by the circumstances surrounding the circulatory collapse.

If the diagnosis appears to be confirmed by the initial response of the patient to therapy, by the blood steroid values, or by history, then an intravenous drip containing 1,000 cc. of 5% dextrose in isotonic sodium chloride solution, to which is added another 100 mg. of hydrocortisone sodium succinate, is continued, and 100 mg. of cortisone acetate is injected intramuscularly. With the termination of the intravenous infusion, the patient is given 50 mg. of cortisone acetate intramuscularly or orally every 8 hours for the subsequent 24 hours, then every 12 hours for the next 24 hours, and then a total of 50 to 75 mg. per day by mouth in two or three divided doses or intramuscularly by injection. During this period, in conjunction with the large doses of hydrocortisone and cortisone plus isotonic sodium chloride solution given intramuscularly, no salt-retaining hormone is necessary. When the dose of cortisone is reduced below 75 mg. daily, the use of supplementary saline solution or a salt-retaining hormone, either desoxycorticosterone acetate intramuscularly or fludrocortisone orally, may be required.

Chronic Primary Adrenal Cortical Insufficiency, Including Addison's Disease

A definite diagnosis of adrenal cortical insufficiency should not be made until a lack of response to intravenously administered corticotropin has been demonstrated, since in the presence of certain abnormal states, such as sarcoid and rheumatoid arthritis, intramuscularly administered corticotropin may not reach the adrenal cortex in adequate concentration. One may follow the urinary steroids or the blood steroid values. The authors prefer the former as being, in general, a more reliable measure of adrenal cortical reserve. The response to corticotropin is also useful in differentiating primary adrenal insufficiency from that secondary to pituitary failure (fig. 2). Blood corticotropin values will be elevated in untreated patients with primary adrenal cortical insufficiency and low or absent in those with pituitary insufficiency.

Hormone therapy is indicated in any patient with impaired adrenal cortical reserve who exhibits weakness, weight loss, gastrointestinal symptoms, hyperpigmentation, fasting hypoglycemia, hypotension, abnormal electronencephalographic tracing, or in whom an abnormal response to a water load may be demonstrated. All patients with chronic adrenal deficiency will exhibit improved biochemical and physiological response to stress when given cortisone or one of its derivatives. Whether supplementary sodium chloride or a salt-retaining hormone is required in addition, and how much, will be determined by the patient's blood pressure, cardiac status, serum sodium and potassium levels, hematocrit value, and changes in body weight. The authors prefer to use a small dose of salt-retaining hormone in most patients with Addison's disease unless increasing age, with a rise in blood pressure, or renal and cardiac changes contraindicate.

Cortisone or hydrocortisone by mouth provides the basic maintenance therapy in a dosage of 25 to 50 mg. daily. For most patients one-half to two-thirds of the daily dose is given on arising, the remainder late in the afternoon. Supplementary hormone (50 to 100 mg. daily) is given in the presence of infection or unusual stress. If nausea or vomiting occurs, cortisone may be given intramuscularly; in an acute crisis, the intravenous administration of hydrocortisone is mandatory, as outlined in the foregoing section. The presence of healed or active tuberculosis is no contraindication to cortisone therapy, although the authors limit the maintenance dose to 20 to 25 mg. per day in conjunction with chemotherapy. Under the circumstances, the usual maintenance dose is well tolerated and may even accelerate recovery of the patient.

Adequate cortisone therapy should induce a regression of pigmentation and a gain in weight; hypoglycemic manifestations should be controlled; and a normal diuresis after a water load should be evident. Abnormalities in the electrocardiogram and electroencephalogram should disappear. Initially, chronically deficient patients may exhibit euphoria and an undesirable psychological response to cortisone, so that a dose not exceeding 12.5 mg. per day may be all a patient can comfortably tolerate. Later the dose may be increased slowly to 25 mg., without untoward symptoms. Patients with preexisting peptic ulcer may experience difficulty in tolerating 25 mg. daily of cortisone or its equivalent. In the rare combinations of diabetes mellitus and adrenal cortical insufficiency, it is preferable to use a normal maintenance dose of cortisone (25 to 37.5 mg. daily) and sufficient insulin to maintain normal glucose levels. It is desirable for these patients to take part of their cortisone late at night or very early in the morning.

Most patients with chronic adrenal cortical insufficiency will be on maintenance therapy with cortisone or hydrocortisone. There is no advantage in using a preparation which is less salt-retaining, i.e., prednisone or triamcinolone. In fact, for a few patients, cortisone or hydrocortisone alone with a generous dietary sodium intake may avoid the necessity of supplementary sodium-retaining hormone.

Most patients will do better on a small dose of sodium-retaining hormone. For this purpose, one has three choices: (1) fludrocortisone acetate by mouth in single daily dose of 0.1 to 0.2 mg.; (2) desoxycorticosterone acetate in oil, the daily intramuscular dose being 1 to 5 mg.; or (3) desoxycorticosterone trimethylacetate, a monthly intramuscular injection of 25 to 75 mg. At a dose level of 0.1 to 0.2 mg. daily, the cortisone equivalent of fludrocortisone can be disregarded, i.e., it will not amount to more than 5 mg. of cortisone equivalent or hydrocortisone equivalent. If larger quantities of fludrocortisone are required, i.e., 0.5 mg. or more, then the cortisone equivalent of the sodium-retaining compound must be considered.

The majority of the authors' patients are on maintenance therapy with either 0.1 to 0.2 mg. of fludrocortisone administered orally daily or 25 to 50 mg. of the long-acting desoxycorticosterone ester given intramuscularly every two to four weeks. Because of the ease with which the oral administration of fludrocortisone can be manipulated, there is a growing tendency to substitute this therapeutic regimen for the monthly injections of long-acting desoxycorticosterone derivatives. Desoxycorticosterone acetate, with a duration of action of 12 to 24 hours, is a useful preparation for a patient who is experiencing nausea, vomiting, or diarrhea in which maximum sodium retention is desirable and in which oral medication may not be well tolerated. A dose of 5 to 10 mg. daily (1 to 2 cc.) of the oil solution given intramuscularly will ensure adequate sodium retention in the presence of normal kidney function. In all instances, it is desirable to establish the optimum dose of sodium-retaining hormone by carefully following changes in body weight, blood pressure, heart size, and serum sodium and potassium levels.

In summarizing, the conditions of the majority of patients with primary chronic adrenal cortical insufficiency will be well maintained on a program which includes 25 to 50 mg. daily of cortisone or hydrocortisone and 0.1 to 0.2 mg. of fludrocortisone by mouth. In the presence of complications, the dose of cortisone should be increased immediately.

Chronic Secondary Adrenal Cortical Insufficiency (Hypopituitarism)

In the presence of anterior pituitary deficiency, adrenal cortical insufficiency is modified in three essential respects. First, pigmentation is unusual, due presumably to the fact that corticotropin and melanocyte-stimulating hormone are not present in increased quantities. Secondly, the manifestations of adrenal cortical insufficiency may be tempered significantly by concomitant thyroid and gonadal deficiencies. And thirdly, since corticotropin does not exert the same primary control over aldosterone secretion as it does in the case of the adrenal 17-hydroxysteroids, sodium deficiency may be less pronounced or nonexistent, a fact consistent with relatively normal urinary aldosterone values in patients with pituitary insufficiency. For practical purposes, one treats adrenal, thyroid, and gonadal deficiencies simultaneously in chronic anterior pituitary deficiency. One could employ corticotropin in these patients, but the practical disadvantages of a daily intramuscular injection of hormone favor the use of cortisone or hydrocortisone given orally. The doses of thyroid and cortisone are advantageously increased or decreased simultaneously, as the patient's cortisone requirements may increase with an increased dose of thyroid. Sodium liothyronine (Cytomel), also known as sodium L-triiodothyronine, may have an advantage over thyroid extract or thyroxin in some patients. The dose of cortisone or hydrocortisone in patients with chronic pituitary insufficiency is generally somewhat less than that for patients with Addison's disease. However, in the presence of unusual stress, a large supplement of cortisone will be required.

Iatrogenic Adrenal Insufficiency

Patients who receive prolonged steroid therapy for diseases such as rheumatoid arthritis, disseminated lupus, pemphigus, and asthma may develop temporary or even permanent adrenal cortical inhibition. Presumably the action of the steroids is to depress the hypothalamic-pituitary system. Withdrawal of hormone therapy may precipitate a relapse of the underlying disease, or, if adrenal function is severely inhibited, it may precipitate an acute adrenal crisis. One of the problems encountered in reducing or terminating steriod therapy in such patients is the difficulty of measuring reserve adrenal cortical function without discontinuing therapy.

Today, with availability of such highly active steroids as fludrocortisone, it is possible to substitute this compound for cortisone or prednisone (i.e., 1 mg. of fludrocortisone for 25 mg. of cortisone or 5 mg. of prednisone) and carry out an adrenocorticotropin test, using the urinary steroid response (17-hydroxysteroids and 17-ketosteroids) as the measure of responsiveness. In this test, corticotropin should be given intravenously (25 units over an eight-hour period is suggested) for at least three days. The small quantity of metabolites of fludrocortisone will not affect the significance of the urinary values. However, when fludrocortisone is used, because of its intense sodium-retaining potency, dietary sodium chloride should be rigidly restricted, but 2 to 6 Gm. of potassium chloride daily may be given. The period of trial should be kept as short as possible, and a mercurial diuretic or chlorothiazide (Diuril) may be given if excessive fluid retention occurs.

Failure to observe an adequate response to intravenously administered corticotropin, although not necessarily indicating permanent adrenal atrophy, certainly suggests that hypoadrenalism will complicate withdrawal of steroid therapy. Unfortunately, an adequate response to corticotropin does not necessarily indicate that the patient's own hypothalamic-pituitary system will secrete an adequate quantity of corticotropin when steroid therapy is discontinued. At present, there is no practical way of deciding this point without careful withdrawal of steroid therapy and an analysis of baseline urinary steroid values.

This discussion naturally raises the problem of whether one should employ corticotropin therapy, intermittently throughout the course of prolonged steroid therapy, in order to prevent or minimize severe adrenal atrophy. It is true that the adrenal responsiveness may be maintained by such a technique, but unfortunately such a procedure will in no way minimize the hypothalamic or pituitary inhibition which may be the more serious problem. Recent studies have indicated that in disease states, such as asthma, adrenal cortical inhibition may be significantly modified by alternating a high dose of steroids for one to two days with a respite of one to two days, without loss of clinical regulation. This technique has not been applied systematically, nor has the adrenal response been studied accurately in other disease states. However, the program deserves further investigation.

Cushing's Syndrome

The clinical manifestations of Cushing's disease (pituitary basophilism) and those of Cushing's syndrome (adrenal cortical hyperfunction) are due to the production of an increased amount of adrenal steroids. The object of treatment is to decrease or eliminate the abnormal hormone secretion. This can be accomplished with certainty by complete removal of a tumor or of both adrenals if hyperplasia is present, theoretically by chemical inhibition of the pituitary-adrenal secretions or the blocking of the end-organ responsiveness to these hormones, and by ablation (surgery or radiation) of the pituitary when it is the primary site of the disorder.

Cushing's syndrome should be considered in every patient presenting hypertension, diabetes, osteoporosis, or skin manifestations characterized by ecchymoses and striae. Psychological manifestations are also a prominent aspect of the disorder. Definite diagnosis rests upon detecting a tumor of the pituitary, adrenal, or ovary and the demonstration of an abnormal steroid excretion in the urine. The response to corticotropin and the character of the steroid excretion pattern may prove helpful in suggesting a histological diagnosis, i.e., carcinoma vs. adenoma vs. hyperplasia.

Cushing's syndrome is a serious but usually remediable disorder. It is unfortunate that many patients are permitted to progress to the point that therapy designed to correct the adrenal hormone secretion may not restore the individual to health becaue of complicating factors such as osteoporosis and fractures, permanent diabetes, hypertension, or severe psychological changes. For this reason, an early and a more radical approach to treatment is to be encouraged.

Tumor of the pituitary is demonstrated rarely. Radiation

to the pituitary in such cases should be tried initially unless local pressure signs from the tumor (impairment of vision, headaches) indicate the need for immediate surgical intervention. If irradiation is carried out, there is no need for supplementary hormone therapy; if hypophysectomy is done, the patient should be carried through the operation with substitution therapy, as outlined in the section on acute adrenal crisis. The postoperative care will be that of a pituitary-deficient patient. In the case of removal of a tumor of the adrenal or ovary, the same hormone substitution program is utilized during or after surgery, as outlined in the section on acute adrenal crisis. However, during the immediate postoperative period after removal of a tumor of one adrenal, corticotropin should be tried, with urinary steroid measurements, to determine whether the remaining adrenal cortical tissue will function adequately.

In the presence of bilateral adrenal hyperplasia, the choice lies between an attempt to control the disease by pituitary irradiation, a subtotal adrenalectomy (usually removing one adrenal completely and two-thirds to three-fourths of the second adrenal) or complete bilateral adrenalectomy. The "cures" from irradiation of the pituitary alone are relatively infrequent and unpredictable but can be spectacular. Since several months must elapse before final evaluation of irradiation treatment can be made, it would seem wise to reserve irradiation for those patients in whom the disease is relatively mild and in whom one can be almost certain that tumor exists. As regards the choice of complete or subtotal adrenalectomy, the authors strongly favor the former, since recurrence of the disease is frequent when any adrenal cortical tissue remains and since in practice one must be prepared for adrenal insufficiency, at least in tthe presence of stress, in the majority of patients with a small remnant of tissue. Experience alone and the seriousness of the disease in the individual patient must weight the judgment of the physician and surgeon in determining the risk of recurrence if any tissue is left and the certainty of adrenal cortical insufficiency if all tissue is removed.

In recent years the development of hyperpigmentation, despite a level of cortisone adequate for all other needs, has been observed in certain adrenalectomized patients. This may occur in association with progressive enlargement of the sella turcica. Whether irradiation of the pituitary, carried out prior to or after adrenalectomy, will prevent or correct this evidence of excessive corticotropin or secretion of the melanocyte-stimulating hormone remains to be seen.

After adrenalectomy in patients with Cushing's syndrome, the dosage of cortisone or hydrocortisone must be followed carefully. Too rapid reduction may result in symptoms of acute adrenal insufficiency in a patient whose tissues have adjusted over the years to a relative excess of hormone. On the other hand, the prolonged administration of excessive doses of cortisone may accentuate the symptoms of Cushing's syndrome. With a good urine output, patients should be given generous quantities of potassium during the immediate post-operative period, i.e., at least 40 to 80 mEq. per 24 hours. In general, the dose of cortisone will be 300 mg. on the day of operation, 200 mg. on the first postoperative day, 150 mg. on the next, then 100 mg. for two to three days, 75 mg. for one week, and, finally, 50 to 62.5 mg. daily for an indefinite period. When the dose of cortisone is reduced below 75 mg. per day in the bilaterally adrenalectomized patient, additional salt or supplementary sodium-retaining hormone will be required, i. e., 1 to 5 mg. of desoxycorticosterone acetate given intramuscularly once daily or 0.1 to 0.2 mg. of fludrocortisone orally. Potassium supplementation, 3 to 6 Gm. daily, if tolerated, and testosterone propionate (25 mg. weekly for female patients) should be continued indefinitely if tolerated.

Adrenal Virilism and the Adrenogenital Syndrome

The clinical manifestations of excessive adrenal androgen secretion may be caused by a tumor or hyperplasia of the adrenal cortex. Steroid analysis of the urine, particularly the 17-ketosteroids, and fractionation of the 17-ketosteroids into those derived from hydrocortisone and those derived from adrenal androgens will be of specific diagnostic aid. Studies on the inhibition of adrenal androgen by cortisone or its derivatives, preferably prednisone or fludrocortisone, will be of additional help in differentiating tumor from hyperplasia and indicating whether medical therapy, i. e., long-continued cortisone therapy, is therapeutically feasible or whether surgery must be resorted to if the disorder is to be cured. The use of the most potent cortisone-like substances in the suppression test is to be encouraged, since the small quantity of ketosteroids derived from the exogenously administered hormone will not interfere significantly with the evaluation of the test. It is helpful to note that prednisone is not excreted as 17-ketosteroid material and hence can be advantageously used. This substance does, of course, give rise to increased 17-hydroxysteroid material in the urine.

Patients with virilism or the adrenogenital syndrome may display evidence of deficiency of sodium-retaining hormone. Under these circumstances, the clinical picture may be complicated by the presence of hypotension, weakness, small heart size, azotemia, hyponatremia, and hyperkalemia. The use of fludrocortisone (0.1 to 0.2 mg. daily by mouth) or a biweekly or monthly injection of the long-acting desoxycorticosterone trimethylacetate given intramuscularly (25 to 50 mg.) should provide satisfactory regulation. The dosage will, of course, be adjusted to maintain a normal blood pressure and electrolyte balance.

If a tumor is suspected in a patient with virilism or adrenogenital syndrome, surgery is advised; the care of the patient is similar to that outlined under Cushing's syndrome, with the exception that the cortisone dosage may be reduced much more rapidly postoperatively since hypercorticism was not present initially. A trial with corticotropin is essential, however, to test the adequacy of the remaining adrenal tissue before supplementary hormone is withdrawn completely. There is usually no need for potassium medication, testosterone, or sodium-retaining adrenal steroid therapy.

The problem is more difficult when virilization or adrenogenital syndrome is due to bilateral adrenal hyperplasia. If adequate suppression can be obtained with a dose of cortisone or cortisone-like steroid which will not induce the undesirable side-effects of Cushing's syndrome, medical management is feasible. Cortisone or hydrocortisone given intramuscularly is recommended for the initiation of treatment, i. e., 100 mg. daily for adults and older children; 25 mg. daily will suffice for infants. The minimum dosage required subsequently will be determined on the basis of the 24-hour urinary ketosteroid excretion. An effort should be made to maintain the level of 17-ketosteroids below 2 mg. in infants, below 7 mg. in older children, and below 10 mg. in adults. Infants will require 25 to 37.5 mg. of cortisone intramuscularly every three or four days; older children will require 50 to 100 mg. every three or four days. The dosage of hormone given orally will be two to three times that employed intramuscularly. The excreted products (17-ketosteroids) from the administered hormone will complicate the interpretation of the suppressive action of the therapy unless substances such as prednisone are used.

It is desirable to use supplementary potassium medication, i. e., 3 to 6 Gm. of potassium chloride daily, in an effort to minimize the hypochloremic, hypokalemic alkalosis which is so characteristically induced by long-term steroid therapy. The return of normal menstrual periods, the disappearance of acne, the regression of body hair, and the attainment of a normal female configuration comprise the criteria of success. Unfortunately, the inhibition of excessive hair growth may be very difficult to attain with steroid therapy.

In the event that suppression of androgen secretion cannot be obtained with a dose of cortisone-like steroid, which in turn does not induce Cushing's syndrome, one is faced with

a difficult decision. Should one proceed with adrenal resection? In contrast to the approach to a patient with Cushing's syndrome, which is in itself life-threatening from a clinical viewpoint, mild virilism or the adrenogenital syndrome is not life-threatening, except in its serious psychological implications. If surgery is undertaken, the following steps are suggested:

1. Unless the adrenals are approached by an abdominal incision which permits the exploration of the ovaries, a pelvic exploratory operation or a culdoscopy with visualization of the ovaries must be undertaken before adrenal surgery. Such an initial step will permit the physician to evaluate ovarian function and the possibility of ovarian disease and to exclude the ovary as a source of androgen-secreting tissue.

2. In contrast to the approach to a patient with Cushing's syndrome in which radical bilateral complete adrenalectomy is to be encouraged, the patient with adrenal hyperplasia and the adrenogenital syndrome would do well to have one adrenal removed and only a portion of the second, in the hope that control of the syndrome might be accomplished by a more conservative procedure. No great difficulty should be encountered if a second, complete adrenalectomy is ultimately deemed necessary. The operative and postoperative needs for hormone therapy will be similar to those noted previously. Again, if a subtotal adrenalectomy is performed, a response to corticotropin should be undertaken prior to discontinuing supplementary hormone therapy. Of course, if sodium-retaining hormone had been required preoperatively, it will be necessary to continue this therapy. In addition, patients with unilateral adrenal removal and partial resection of the second gland may require supplementary sodium chloride or sodium-retaining hormone (fludrocortisone) by mouth once daily, desoxycorticosterone trimethylacetate given intramuscularly once monthly, or desoxycorticosterone acetate in oil, intramuscularly for daily use.

Finally, no patient with menstrual irregularities and a virilizing syndrome should have her adrenal explored (in the absence of a securely documented, unilateral adrenal mass) until ovarian exploration has been carried out. A deficiency of mineralocorticoids should also be excluded in all adrenogenital cases.

Primary Hyperaldosteronism (Conn's Syndrome)

All patients with hypertension, with unexplained episodes of weakness, with unexplained hypochloremic, hypokalemic alkalosis, and with unexplained polyuria and palydipsia should be screened for primary hyperaldosteronism. The majority of patients with primary hyperaldosteronism do not exhibit edema. The latter finding is characteristic of secondary hyperaldosteronism. A definitive diagnosis of primary hyperaldosteronism may be difficult to establish, because urinary aldosterone determinations are difficult to carry out, and normal values have been encountered in well-documented cases. It was hoped that a determination of the salivary sodium:potassium ratio, which can be easily measured, might provide a readily available screen for cases of primary hyperaldosteronism, since aldosterone is known to affect the sodium concentration of saliva. At present it can be stated that a value of more than 0.5 in salivary sodium: potassium ratio is strong evidence against excessive aldosterone secretion at that time. (The test is carried out in the morning, with care being taken that no dentifrice or other sodium-containing medication has been used; the analysis is made on the second 10-minute specimen with paraffin chewing, the first 10-minute specimen having been discarded.) Values of less than 0.5 are frequently found in secondary hyperaldosteronism and probably in other conditions. Whether the salivary sodium:potassium ratio will assist in excluding the many patients who do not need definitive hormone studies remains to be seen. Of course, every patient with unexplained hypertension should have pyelograms, which may prove helpful in detecting a large tumor. Unfortunately, small tumors or bilateral adrenal hyperplasia are not likely to be detected by this means.

The diagnosis of primary hyperaldosteronism should be considered seriously in the presence of hypertension and hyperchloremic, hypokalemic alkalosis with a normal potassium content of the urine, i. e., 40 to 50 mEq. or more per 24 hours. Sodium restriction and potassium medication should ameliorate the symptoms, whereas unrestricted sodium and low-potassium intake should aggravate the disorder. Changes in the electrocardiogram, suggesting hypokalemia, may initiate the search for the disorder in patients with hypertension and cardiac abnormalities.

Since primary hyperaldosteronism is a life-threatening disorder, an active and aggressive attitude should be taken toward the diagnosis and treatment of the syndrome. The removal of a tumor presents no unusual therapeutic problems except that a generous potassium supplement should be provided preoperatively and postoperatively. An aldosterone-secreting tumor will inhibit the production of aldosterone by the opposite adrenal but will not inhibit the adrenal secretion of 17-hydroxysteroids and androgenic steroids. Postoperatively, one must watch for excessive sodium loss and be prepared for the administration of supplementary sodium salts or salt-retaining hormone as needed. In the absence of a tumor, a complete bilateral adrenalectomy may be necessary in a patient with hypertension and unexplained hypokalemia. Histological examination of the adrenals, certainly frozen sections, may not prove helpful in guiding the surgeon.

The operative and postoperative care of such patients, as far as adrenal hormone replacement is concerned, is identical with that previously described. However, since hypercorticism did not exist preoperatively, one may attain normal cortisone-replacement levels relatively rapidly after operation. Again, hypokalemia is probably the most serious immediate postoperative complication. One note of caution should be mentioned. Since patients with this condition may lose sodium rapidly and in large quantities postoperatively, if unsupervised, the patient may develop hyperkalemia as a consequence of excessive sodium loss and supplementary potassium medication at a time when his body tissues are markedly depleted of potassium. Daily serum sodium and potassium determinations are essential in the immediate postoperative management of these patients.

Secondary Hyperaldosteronism

The syndrome of edema, associated with increased urinary values for aldosterone, implies a casual relationship between secondary hyperaldosteronism and the edematous state. Four points deserve consideration. 1. An increase in urinary aldosterone excretion does not necessarily, but in all probability does, imply increased aldosterone production. 2. It has been shown that patients with heart failure and generalized edema may have normal aldosterone values until treatment is instituted. 3. A decrease in aldosterone excretion has been attained with adrenal inhibition, without a concomitant increase in sodium excretion, suggesting that, in such cases, secondary hyperaldosteronism was not at that particular time the determining factor in the production or maintenance of the edematous state. 4. A decrease in aldosterone excretion produced by inhibition of adrenal secretion or the administration of a competitive substance has resulted in a sodium diuresis in certain patients with edema and elevated urinary aldosterone values. In these patients it is presumed that secondary hyperaldosteronism has been an important factor in the genesis or maintenance of the edematous state. Finally, adrenalectomy in certain patients with edema has been followed by a sodium diuresis and marked clinical improvement in patients with hypertensive cardiovascular disease, the nephrotic syndrome, and cirrhosis with ascites.

From these considerations there is little doubt that secondary hyperaldosteronism is a frequent concomitant of the

edematous state. There is considerable uncertainty as to its importance at any given stage in a patient's decompensation. Medical inhibition of aldosterone production or competition with the action of aldosterone on renal tubular mechanisms would appear to be the most promising approach to the clinical problem. Bilateral complete adrenalectomy for secondary hyperaldosteronism should be reserved for those patients in whom a direct relationship between sodium retention and hypersecretion of aldosterone can be demonstrated, and in whom the risk of major surgery may be justified by an important degree of or prolonged clinical benefit. The specific hormone requirements for the management of such patients will be similar to those employed in other cases of bilateral adrenalectomy, with the exception that cortisone-like steroids of less sodium-retaining capacity, i. e., prednisone and triamcinolone, will, in general, be preferred during the postoperative period.

Pheochromocytoma

Recent advances in the chemical determination of catechol amines in the blood and urine have provided definite techniques for detecting the presence of pheochromocytoma in patients presenting paroxysmal or sustained hypertension, particularly when associated with anxiety, dizziness, palpitation, nausea, vomiting, sweating, precordial pain, and peripheral vasoconstriction.

After the demonstration of a tumor or elevated levels of urinary or blood catechol amines, surgical exploration should be undertaken. The use of intravenously administered phentolamine (Regitine) methanesulfonate prior to and during operation may be lifesaving in preventing an excessive rise of blood pressure. A solution of this substance should be available throughout the operation. Later with the ligation of adrenal vessels and the removal of a tumor, one must be prepared for a sudden and precipitous fall in blood pressure. This may be corrected by the use of levarterenol (Levophed) bitartrate given intravenously (never subcutaneously or intramuscularly). Phenylephrine (Neo-Synephrine) hydrochloride may be given subcutaneously to correct mild hypotensive episodes. Perhaps the most important postoperative maneuver is to keep the patient undisturbed for several hours on the operating-room table, as a sudden change in posture may precipitate collapse. Postoperatively, adrenal steroid therapy is not required unless a bilateral adrenalectomy has been performed. Postoperatively, the blood pressure can be controlled with phenylephrine. In the more severe cases it may require 48 to 72 hours before supportive medication can be withdrawn.

This study was supported, in part, by grants from the Eugene Higgins Trust, Harvard Medical School, and the John A. Hartford Foundation, New York.

J. Am. Med. Assoc. 168:2130 (Dec. 20) 1958.

PACK MINIMS STERILE

STERILE PACK MINIMS

Absolute sterility of all surfaces of the Minims unit is assured by the pliofilm overwrap.

Minims units for each drug contain the quantity sufficient for usual administration of that particular drug.

Ophthalmic drugs available in the Minims package:

ATROPINE SULFATE 1%
ATROPINE SULFATE 2%
ESERINE SALICYLATE 0.5%
ESERINE SALICYLATE 0.25%
PILOCARPINE HCl 1%
PILOCARPINE HCl 2%
FLUORESCEIN SODIUM 2%
HOMATROPINE HBr 2%
HOMATROPINE HBr 5%
PHENYLEPHRINE HCl 2.5%
PHENYLEPHRINE HCl 10%
SCOPOLAMINE HBr 0.2%
TETRACAINE HCl 0.5%

MINIMS... a particularly valuable administration unit for...

SURGERY
HOSPITAL WARDS
INDUSTRIAL MEDICINE
EMERGENCY ROOMS
OPHTHALMOLOGICAL OFFICES
PATIENT USE

For further information or literature write or phone:

MINIMS®
STERILE OPHTHALMIC DROPS IN DISPOSABLE UNITS

Minims solutions remain stable for an indefinite period.

Barnes-Hind
895 KIFER ROAD · SUNNYVALE, CALIF.
REgent 6-5462

POSITIONS

in hospital pharmacy

. . . . . .

The Personnel Placement Service is operated without charge for the benefit of hospitals and pharmacist members of the American Pharmaceutical Association and the American Society of Hospital Pharmacists. The ultimate purpose is the improvement of pharmaceutical services in hospitals, by more adequately fulfilling hospital pharmacy personnel needs and by locating positions which provide challenging opportunities for pharmacists who have indicated an interest in a hospital career.

By participating in the service, the hospital indicates a desire to achieve a pharmaceutical service which meets the Minimum Standard for Pharmacies in Hospitals. A description of the position should be submitted to the Division of Hospital Pharmacy on the forms provided. The hospital will receive applications directly from the applicant. The hospital agrees to reply to each application received and to notify the Division of Hospital Pharmacy when the position is filled.

The pharmacist, by participating, agrees to submit a Personnel Placement Service Information Form to the Division of Hospital Pharmacy. The applicant will then be notified of openings listed with the Service as they become available and can negotiate directly with the hospital if he is interested. It is agreed that the Division of Hospital Pharmacy will be notified as soon as a position is accepted.

A listing of positions open and wanted will be made regularly in the American Journal of Hospital Pharmacy without charge. Neither the name of the hospital offering the position nor the name of the applicant will be listed, except by code. All inquiries should be directed as shown below, including the code number.

Address all inquiries to
Division of Hospital Pharmacy
2215 Constitution Avenue, N. W.
Washington 7, D.C.

positions open

Chief Pharmacist—350 bed hospital. Must be eligible for licensure in N.J.; interest in manufacturing; 44-hour week, 2 weeks' vacation. Salary $5200-$5700. PO-6

Staff Pharmacist—550 bed general hospital located in Ohio. 40-hour week; 2 weeks' vacation. Salary $400-$450. PO-34

Asst. Chief Pharmacist—310 bed general hospital located in Va. 40-hour week, 2 weeks' vacation, 3 weeks' sick leave, 6 holidays. Salary $5,000 to $6,000. Also
Staff Pharmacist—259 bed hospital located in Va. Hospital experience preferred. 40-hour week, 2 weeks' vacation. Salary open. PO-35

Staff Pharmacist—460 bed general hospital in Mass. 40 hour week 2 weeks' vacation; other benefits. PO-40

Asst. Chief Pharmacist—Large voluntary hospital located in Brooklyn; N.Y. registration required. Supervisory ability needed. 35-hour week, 2 weeks' vacation, 10 days' sick leave, 9 holidays. PO-51

Chief Pharmacist—88 bed hospital located in Pa. Planning expansion to 125 beds for general patients and 40 beds for chronic patients. Possibility for pharmacist to serve as Asst. Administrator in charge of Purchasing, Central Supply and Store Room. 40 hour week; 2-4 weeks' vacation. Young man preferred. Salary open. PO-59

Staff Pharmacist—325 bed research hospital. Min. 2 years' experience preferably in hospital pharmacy. N.Y. registration required. Manufacturing sterile solutions and assisting in product development. Salary $4770-$5860 plus benefits. Research work beyond 40-hour week available at $3.00 per hour. PO-61

Asst. Chief Pharmacist—100 bed general hospital. Ind. registration required. Young lady preferred. Hospital experience not necessary. Main area of responsibility in Central Supply and Solution Manufacturing. 40 hour week, 3 weeks' vacation. PO-63

Pharmacist—Animal hospital located in Colo. Duties include maintaining drug stock and checkout service, also willing to help students. 44 hour week, 4 weeks' vacation. Salary $5,000. PO-64

Chief Pharmacist—325 bed general hospital. Eligible for registration N.Y. Hospital experience desirable but not necessary. 40-hour week, 2 weeks' vacation. Salary dependent upon qualifications. PO-70

Asst. Chief Pharmacist—313 bed general hospital. Eligible Ky. registration. Previous hospital experience not necessary. 40-hour week, 2 weeks' vacation. Salary $400-$500, benefits. PO-73

Chief Pharmacist—265 bed general hospital. Varied duties including teaching if interested. No experience required. 40-hour week, 2 weeks' vacation. Salary $400 (approx.) plus benefits. PO-74

Staff Pharmacist—335 bed hospital located in Fla. Duties include responsibilities in outpatient department and parenteral solution room. 40-44 hour week, 2 weeks' vacation; 1 meal daily. Salary $5200. PO-75

Asst. Chief Pharmacist—237 bed general hospital in West Va. Female desired. 44-hour week; 2 weeks' vacation. PO-77

Staff Pharmacist—503 bed general hospital. Inpatient and outpatient prescriptions; manufacture of some injectibles. Male or female. Interested in recent graduate with hospital experience desirable but not required. 40-hour week; 2 weeks' vacation; other benefits. PO-78

Chief Pharmacist—320 bed general hospital located in Iowa. Experience or internship in hospital pharmacy required. 40-44 hour week, 2 weeks' vacation, other benefits. Salary open. PO-80

Staff Pharmacist—316 bed general hospital. Eligible registration in Minnesota. Some manufacturing; 40-hour week 2 weeks' vacation; other benefits. Salary open. PO-81

Staff Pharmacist—295 bed hospital expanding to 500 in future. Eligible for registration in Mich. Experience in hospital pharmacy and manufacturing preferred. 40-hour week, 2 weeks' vacation. Salary $5720. PO-86

Asst. Chief Pharmacist—325 bed hospital; 40 hour week; 4 weeks' vacation; salary $5,000. Must be eligible for registration in Pa. PO-89

Chief Pharmacist—400 bed general hospital. B.S. required. Internship in hospital pharmacy preferred. Eligible for Tex. registration. 40-hour week, 2 weeks' vacation. Salary up to $6,000 to start. PO-90

Pharmacist—Female, Filipino, recent graduate Manila Central Univ. Would like to locate in western part of U. S. PW-127

Pharmacist—Male, married. Registered Mass., D.C. and Md. Will locate any part of U. S. Served hospital pharmacy internship. Over 20 years hospital pharmacy experience. PW-128

Staff Pharmacist—Male, married. Several years hospital pharmacy experience. Registered Mich. PW-129

Asst. Chief Pharmacist—Male, single, registered Neb. and Pa. Background of hospital and retail pharmacy. Has M.S. pharmacy. Desires Midwest location. PW-133

Staff Pharmacist—Female, married, registered Kansas. 4 years hospital pharmacy experience. PW-136

Chief Pharmacist—Male, married, registered Ark. B.S. pharmacy. 5 years experience as Chief Pharmacist. PW-137

Asst. Chief Pharmacist in large Hospital or Chief Pharmacist in Smaller Hospital—Available in June. B.S. Chemistry, B.S. Pharmacy, M.S. Hospital Pharmacy. Completing internship at Johns Hopkins Hospital. Single; completed military obligation. Will locate anywhere. PW-138

Chief Pharmacist—Male, married. Registered Wis. PhD. Several years hospital pharmacy experience. Locate any section of the country. PW-139

Chief Pharmacist—Male, married. B.S. Conn. registration. 5 years hospital pharmacy experience. Prefers Northeast section of country. PW-140

ASST. CHIEF PHARMACIST—315 bed general hospital. Registration in Iowa required. Experience desirable but not essential. 40-hour week, 2 weeks' vacation. Salary $450. PO-92

ASST. PHARMACIST—360 bed general hospital, located in N. J. Prefer graduate of hospital internship program. 40-hour week. Salary $90. PO-93

STAFF PHARMACIST—500 bed general hospital located in Okla. B.S. required. 40-hour week, salary open. PO-95

STAFF PHARMACIST—400 bed general hospital. Eligible registration in Fla. 40-hour week, salary open. PO-96

CHIEF PHARMACIST—425 bed hospital. Male preferred. Mo. registration. Will train good applicant without experience. 40-hour week. Salary open. PO-98

CHIEF PHARMACIST—200 bed general hospital. Male or female considered. Prefer hospital experience. Salary $5500. 44-hour week, vacation, sick leave. PO-100

ASST. CHIEF PHARMACIST—152 bed general hospital expanding to 180 beds. Registration in Neb. required. 40-hour week, 2 weeks' vacation. Salary open. PO-101

CHIEF PHARMACIST—73 bed general hospital. Complete responsibility of Pharmacy Dept. 44-hour week, 2 weeks' vacation. Salary open. PO-102

STAFF PHARMACIST—215 bed general hospital expanding to 35 more beds. N. Y. registration required as well as hospital experience. 40 hour week, 2 weeks' vacation. Salary open. PO-104

STAFF PHARMACIST—425 bed general hospital located in Tex. 40-hour week, 2 weeks' vacation. Salary $425-$500. PO-105

CHIEF PHARMACIST—244 bed hospital. California registration required. Complete charge of pharmacy including all purchasing. 40-hour week, 2 weeks' vacation. Salary $505-$613. PO-106

STAFF PHARMACIST—585 bed general hospital located in Ore. one year hospital pharmacy experience required. Salary open. PO-107

positions wanted

CHIEF PHARMACIST—(or Asst. Pharmacist at large hospital); prefers vicinity of St. Louis; now employed as staff pharmacist at hospital. Registered in Mo. PW-13

CHIEF PHARMACIST IN A TEACHING HOSPITAL—Registered Ind., Mich., and Mo.; prefers general hospital in Midwest; experience in teaching and in hospital pharmacy. PW-26

PHARMACIST—Registered in Ohio since 1934; also registered in Vt.; desires to locate in Vt. Experience in retail pharmacy only. PW-27

PHARMACIST—Prefers vicinity of Chicago; registered in Ill., now employed there. Graduate of Univ. of Ill. College of Pharm. PW-31

CHIEF PHARMACIST OR ASST. PHARMACIST—Prefers medium size hospital; registered in Ind., Mich., and Wis. 8 years' experience chief pharmacist and purchasing agent. Prefers Midwest or East. PW-32

PHARMACIST—Male, married; B.S. 4 years' retail experience Army Dispensary. Registered N.Y.; desires to locate in East. PW-44

CHIEF PHARMACIST—M.S. degree in hospital pharmacy; prefers East; male, single; extensive experience, including pharmacy and administrative office in Air Force. PW-62

CHIEF PHARMACIST—Registered in Tenn., La., Tex.; prefers South; graduate Univ. of Tenn., School of Pharmacy. PW-64

PHARMACIST—Prefers small hospital; experience includes 21 years as owner-manager of retail store. PW-65

INDIAN PHARMACIST—Desires appointment to obtain higher training in hospital pharmacy; graduate Madras Univ.; 1½ years' experience in 1,000 bed hospital, including inpatient and outpatient dispensing, parenteral and general manufacturing and administration. PW-68

STAFF PHARMACIST—Female, married; internship at Freedman's Hospital; experience in hospital pharmacy. B.S. Prefers D.C. area. Registered in Ind., D.C. and N.C. PW-72

CHIEF PHARMACIST—Female, single; hospital experience. Desires position 100 bed hospital. B.S. Registered Ky. Prefers Ky. PW-73

HAITIAN STAFF PHARMACIST—Male, married. Has 5 years' hospital experience. Present owner of pharmacy. Desires to locate in northwest U.S. PW-74

STAFF PHARMACIST—4 years' hospital pharmacy experience; prefers Wash. state (registered). Female married, B.S. pharmacy. PW-87

IRANIAN PHARMACIST—Desires opportunity to continue hospital pharmacy studies; single, age 30; excellent academic background; now studying industrial chemistry Columbia Univ. Prefers location in West or Northeast. PW-88

ASST. PHARMACIST—Female, married. Educated and trained in Philippines. Served hospital pharmacy internship. Registered Manila. Desires to locate East Coast of U.S. PW-91

CHIEF PHARMACIST—Prefers small hospital in Ohio. Male, married. B.S.; registered Ohio. Excellent academic and professional background. PW-93

STAFF PHARMACIST OR ASST. CHIEF—Female, single, Filipino, educated and trained Philippines. 10 years' hospital experience. Served hospital pharmacy internship. PW-95

PHARMACIST—Male, married. Registered Ill. Desires to locate in New England. PW-102

STAFF PHARMACIST—Single female, registered Mo. B.S.; hospital pharmacy experienced. Desires locate Midwest. PW-104

CHIEF PHARMACIST—Female, single registered Penna. 12 years' experience Chief Pharm. Desires to locate in Penna. or Ohio. PW-111

CHIEF OR ASST. CHIEF PHARMACIST—Male, married, registered Mich. and Ariz. Served hospital pharmacy internship. Retail experience plus 7 years' hospital pharmacy experience. PW-113

STAFF PHARMACIST—Male, married, registered Mass. Retail and hospital pharmacy experience. Desires locate East or Northeast. PW-114

CHIEF OR STAFF PHARMACIST—Female, single, registered Tex. Desires to locate in East. PW-115

STAFF PHARMACIST—Female, single, B.S. Retail experience only. Registered Fla. PW-116

ASST. CHIEF PHARMACIST—Male, single. B.S. Vet. Adm. Hosp. experience. Registered Va. and Washington, D.C. PW-117

STAFF PHARMACIST—Male, married. B.S. registered La., Va., and Washington, D.C. PW-118

ASST. DIRECTOR OR DIRECTOR OF PHARMACY SERVICES—Male, single, B.S. Retail and 4 years' hospital experience. Registered, Ill. PW-119

ADMINISTRATOR—Male, married, D.Sc. 15 years' hospital pharmacist. Desires locate Fla. PW-120

PHARMACIST—Male, single. B.S. Registered Maine. Served hospital pharmacy internship. PW-122

CHIEF PHARMACIST—Male, single. Registered Conn. and N. J. 10 years' hospital pharmacy experience, B.S. PW-123

CHIEF PHARMACIST—Male, single. 10 years' hospital pharmacy experience. 1 year pharmacy internship. Registered Ariz., Ga., New Mexico, prefers south. PW-124

CHIEF PHARMACIST—Female, single. B.S. 2 years' hospital experience. Registered Ohio. Prefers Ohio or Ill. PW-126

News about controlling pain or cough

New 6-page Review Sums Up the latest findings on one of medicine's most useful but underestimated drugs

Ten minutes is all it will take you to bring yourself completely up-to-date on codeine. Concisely written from the clinical viewpoint, *Codeine Today* quotes the statements of today's authorities on when to use, how to use and where to use this versatile drug. Information is of interest to practically every pharmacist and doctor. Bibliography contains 60 references, more than 90% of which were published in 1958.

SEND FOR YOUR FREE COPY TODAY

MERCK & CO., INC.
Medicinal Products Department
RAHWAY, NEW JERSEY

Please send me____copies of *Codeine Today.*

PHARMACIST'S NAME AND ADDRESS

ADVERTISERS

March, 1959

Abbott Laboratories
Compocillin-VK, 19
Erythrocin, 17
Spontin, 21

Ames Company, Inc.
Albustix; Clinistix; Ketostix; Uristix; Phenistix, 6

Bristol-Myers
Bufferin, 31

Ciba Pharmaceutical Products, Inc.
Esidrix, 8-9
Ritalin, outside back cover
Ritalin, Parenteral, 25
Ritonic, 3

Eaton Laboratories
Furacin, 15

Endo Laboratories
Percodan; Percodan-Demi, 22

Eli Lilly and Company
Darvon Compound, inside front cover

E. Fougera & Company
Orabilex, 23

MacBick Company
Pour-O-Vac, 33

McKesson and Robbins
McKesson Hospital Service Departments, 5

Merck and Company, Inc.
Codeine, 150

Wm. S. Merrell Company
TACE, 4

Organon, Inc.
Liquaemin Sodium, 11

Panray Corporation
Pyridoxine; Parasal Preparations; Prednisone; Isoniazid, 12

Parke, Davis & Company
Carbrital, 102

A. H. Robins Company, Inc.
Robaxin, 10

Roche Laboratories, Div. of Hoffmann-La Roche, Inc.
Konakion, 34

Smith Kline & French Laboratories
Compazine, 29

E. R. Squibb and Sons, Div. of Mathieson Chem. Corp.
Ether, inside back cover

Schering Corporation
Trilafon, 27

The Upjohn Company
Lipomul I.V., 7

Warren-Teed Products Company
Ilopan, 14

West Chemical Products
Wescodyne, 24

Winthrop Laboratories
Alevaire, 16

Wyeth Laboratories
Tubex, 13